

# *The American Journal of* **DIGESTIVE DISEASES**

*An Independent Publication*

**DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION**

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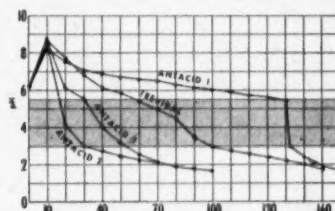
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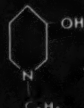
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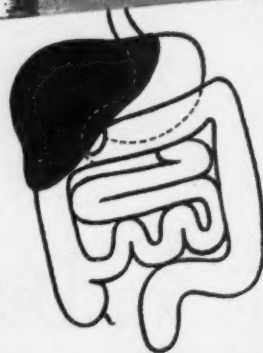
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## THE USE OF CITRUS FLAVONOIDS IN RESPIRATORY INFECTIONS

MORTON S. BISKIND, M. D., Westport, Connecticut  
AND WILLIAM CODA MARTIN, M. D., New York, N. Y.

THE CITRUS flavonoids have been shown to be effective in restoring impaired capillary permeability and fragility (1-3). In the course of administering a preparation containing equal parts of citrus flavonoids and ascorbic acid\* for this purpose it was noted that associated infections cleared up dramatically. In one case, in a patient with influenza, who had a temperature of 102 F. and severe upper respiratory involvement, recovery occurred by crisis within 24 hours after initiating this therapy. There was profuse sweating, the temperature dropped rapidly to normal and the respiratory symptoms simultaneously subsided. Contrary to the usual experience in these cases, there was little or none of the expected subsequent asthenia and the patient reported that he felt "wonderful" the next day. This surprising observation suggested a further trial of the flavonoids in respiratory infections.

We have therefore investigated the effectiveness of these nutritional factors in 22 further cases, ages 7 to 70, ranging from simple rhinitis without elevation of temperature, to acute follicular tonsillitis, and influenza, with fever to 102 F. With only two failures, the initial experience was confirmed. In 20 of these cases, recovery occurred in from 8 to 48 hours, usually in 24 hours. (The two failures were in a child with persistent rhinitis, probably of allergic origin, and in an elderly woman with acute pleurisy.)

In a man, age 26, with acute follicular tonsillitis, temperature 101 F., administration of the flavonoid preparation 200 mg. every three hours, led to recovery by crisis in 48 hours with profuse perspiration, rapid drop in temperature, and subsidence of the pharyngeal lesions.

In another man, age 42, with severe rhinitis, pharyngitis and tracheitis, temperature 101 F., 36 hours after beginning administration of the flavonoid preparation, 200 mg. three times a day, the temperature was normal and sore throat, cough and rhinitis had all disappeared, only some thickened mucus persisting. This occurred despite the fact that, against advice, this patient continued at his work which involved physical exertion and heavy exposure to irritant volatile solvents.

In the case of a man, age 70, who had a severe upper respiratory infection associated with a purulent conjunctivitis, both the respiratory symptoms and the conjunctivitis cleared up in 48 hours on a dosage of 200 mg. three times a day. There was simultaneously

a remarkable sense of well-being, on which the patient commented spontaneously.

In three patients the flavonoids were used twice within two months for severe respiratory infections; recovery occurred each time within 8 to 24 hours. Dosages in this series have varied from 1 capsule (100 mg.) three times a day to 12 capsules a day. It was found that 200 mg. three times a day was the most effective dosage; the larger dosage sometimes produced a feeling of mental "stimulation" without apparently enhancing the anti-infective properties. This was the only side-effect noted. The watery secretion characteristic of acute rhinitis usually thickened rapidly, often in a few hours, and sometimes caused temporary difficulty in nasal breathing; this difficulty soon subsided though the thickened mucus in some cases persisted for several days.

The flavonoids appear to be effective no matter at what stage of the infection therapy is started. The optimum duration of administration has not been determined though it has been our practice to continue the flavonoids as long as the thickened mucus persists. Whether or not the ascorbic acid in the preparation is necessary is under investigation—several of our patients had received ascorbic acid from 300 mg. to 1.5 Gm. per day without apparent benefit, but responded to the flavonoid-ascorbic acid mixture promptly. The fact that the dosage effective in these infections, is identical with that known to restore normal capillary integrity, and the rapid thickening of the nasal secretions which occurs, suggest that the flavonoids operate in the infections by decreasing capillary permeability. However, other anti-infective properties are not excluded, and are being investigated. Possible effects in other types of infection are also being studied.

Though our series of cases is small, the effects have been so dramatic as to warrant publication of this preliminary report, so that others may further assess the citrus flavonoids in infections. Since this is a form of nutritional therapy, it involves a physiologic approach to a group of infections usually unresponsive to any previous type of therapy.

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3. Sokoloff, B. and Eddy, W. H.: Bio-Flavonoids in Radiation Therapy, *ibid.*, 1952, pp. 32.

\*The preparation used in this study was C. V. P.® Each capsule contains citrus flavonoids 100 mg. and ascorbic acid 100 mg. Kindly supplied by Dr. Louis Freedman, Director of Research of the U. S. Vitamin Corporation, New York.

## TWO CASES OF WHIPPLE'S DISEASE

ANTHONY BASSLER, M.D., F. A. C. P., LL.D., New York City.

**M**OST OFTEN designated as intestinal lipodystrophy, Whipple first described a condition as follows. The presentation of Whipple, because of its completeness, is given in full as Whipple presented it. "The following case was characterized clinically by a gradual loss of weight and strength, stools consisting chiefly of neutral fat and fatty acids, indefinite abdominal signs, and a peculiar multiple arthritis. The diagnosis lay between neoplasm and tuberculosis of the mesenteric structures. Pathologically the lesions of interest were found in the intestines and the lymphatic tissue draining this region. The intestinal mucosa showed enlarged villi due to deposits of large masses of neutral fats and fatty acids in the lymph spaces and an infiltration of the interglandular tissues by large mononuclear and polynuclear giant cells. The submucosa in many places shows similar deposit in the enlarged lymph spaces and invasion by large mononuclear cells. The mesenteric glands in gross showed the most striking changes, but under the microscope the picture closely resembled that seen in the intestine. The glands showed the same deposits in even greater amounts, and a chronic inflammatory reaction with replacement of much of the gland tissue by fibrous scar tissue, masses of large mononuclear cells or polynuclear giant cells of the foreign-body type. The lymphatic tissue of the bronchial glands, bone marrow, and lungs showed no abnormalities of importance. The other organs are described below, but no changes were found which seemed related to the intestinal lesions."

In an effort to differentiate the condition from sprue, and to present what appears as two additional cases, added to the about fifty that have been reported in the literature, these two cases are offered.

Plummer et al, summarizing the symptoms in 34 cases as supported by 34 observers, all of which were confirmed by autopsy or laparotomy, showed there were only six females to twenty-eight males. The ages were those of middle life (32 to 60), and the duration of symptoms from six months to eight years. Diarrhea and irritation were present in all, pain and distress came next, and these were followed in diminishing order by arthritis, edema, purpura, hypotension, palpable mass in the abdomen, and skin pigmentation of a mildly bronze-icterus type. On the laboratory side, secondary anemia and achlorhydria were most often found with scattered non-suggestive findings in fecal fat, non-protein and serum protein, calcium, prothrombin, blood glucose, eosinophilia and deficiency pattern on X-ray examination of the small intestine and colon.

The initial symptoms noted clinically were pain or diarrhea in 50%, and polyarthritis in 50%. A watery diarrhea invariably ensued at some time and it is characterized by persistency and inability to control by treatment. Transit jaundice and hemolytic anemia may occur occasionally. Cases have been operated upon on the diagnosis of Hodgkin's disease, Boeck's sarcoidosis, tuberculosis, adenitis and ileitis.

The symptoms as listed by Plummer et al were:

Emaciation	76.4
Hypotension	64.7
Purpura	50.0
Pigmentation	47.
Lymphadenopathy	41.1
Edema	38.2
Abdominal mass	26.4
Fever	17.0
Glossitis	8.8
Tetany	8.8
Arthritis	8.8
Sudden death	29.4

The physical signs usually are indefinite and insidious, although emaciation is an early symptom. An indefinite plastic or doughy mass is a most tangible and significant observation for diagnosis, especially when other symptoms are present.

The laboratory studies are non-specific and consistent with those found in other diarrheal and most nutritional diseases. Secondary anemia is common, about 80%; achlorhydria, about 75%; and increased fecal fat, about 50%. This latter is important because the fat loss is never as high as it is in idiopathic steatorrhea or even in chronic pancreatic disease. Roentgenologic studies showed deficiency pattern in seven of eleven cases and joint changes in two.

Differential diagnosis demands that this disease be distinguished from sprue, sprue-like disorders, pancreatic insufficiency, and other non-fatty diarrheal diseases, abdominal pain and progressive anemia. In the steatorrhea group (sprue, idiopathic steatorrhea, symptomatic sprue and pancreatic disease), differentiating is often confusing. However, geography, absence of hypotension, pigmentation and abdominal masses may be helpful. Fatty stools are more often present in the group just mentioned, and the diarrhea is less watery and bowel movements less frequent. Glossitis is often present in sprue but macrocytic anemia not so pronounced. The symptomatic sprue is due to obstruction of the lacteals or mesenteric glands with blockage, and is separated from lipodystrophy only with much difficulty.

In pancreatic disease pigmentation, very marked diarrhea and pain are usually absent. Amylase and lipase factors are low in duodenal studies, with blood amylase higher than normal. The X-rays may be of help.

Lipodystrophy reveals many characteristics with pituitary and adrenocortical hypofunction, but the pig-

mentation is different and hypotension, asthenia, abdominal pain, steatorrhea and abdominal masses uncommon.

The cause of lipodystrophy is unknown. Previous hypotheses have been refuted and no investigative work having been done, we can only view the disorder on a clinicopathologic basis. Because of its resemblance to symptomatic sprue it probably belongs in that classification, although those who have studied the disease believe it to be an entity by itself. Death usually occurs from one to five years after the onset of symptoms from inanition or some terminal disorder.

Briefly, the microscopic findings may be summarized as follows: The villi of the small intestine are enlarged, the submucosa thickened, and the mesenteric glands enormously enlarged by deposits of neutral fats and fatty acids. With the usual cells there are a large number of cells with a foamy protoplasm, a pale nucleus, and actively ameboid. Ecchymoses are common. The process progresses until glands are packed with fat. The bacteriology is not conclusive although a peculiar rod shaped organism reported in other cases and present in mine may be etiologic. An excellent discussion of the pathology is contained in Whipple's original article.

Referred by Dr. Frank Overton

*Case I.* A 59 year old man was seen in consultation on July 2, 1951. The complaint was extreme fatigue, loss of weight (31 lbs. in 14 months), arthritis and an uncontrollable watery diarrhea, alternating with constipation. He coughed considerably. The X-ray examination of chest and abdomen was judged normal, the red cell count was normal, but the white cell count was high on two occasions (18,500 and 21,000). Two sedimentation rates were 19 and 21. The urine was normal. In a light colored and thin feces there was a slight increase of fat seen as fatty acids. His skin was darkened but not enteric. Oral tolerance test and electrocardiogram were normal. One could feel soft masses in his upper abdomen, especially to the left side of the upper abdomen. Vitamin "K", folic acid and liver extract were given without benefit.

His course was steadily downward. Over a space of seven days effort was made to control a vague pain in his abdomen and the large number of bowel movements with opiates, without avail; and he died seven months after the diagnosis was made with relatives in a western city from, supposedly, "pneumonia and anemia." Unfortunately no autopsy was performed. The case however clinically corresponded to that of Whipple's disease.

Referred by Dr. Shapiro.

*Case II.* Female 69 years of age, mother of four children. Parents' history not relevant. Uterine suspension operation was done 30 years ago. Patient had been well up to six months ago when she began to have abdominal and joint pains. A slow loss of weight took place which continued steadily and consistently, and was 30 lbs. up to the time seen. The diarrhea was continuous, the stools being watery, clay colored and foul smelling. With the start of the illness a cough ensued, the lungs always being clear.

She was a very emaciated woman, having as many

as fifteen watery stools a day. The blood pressure was 150/70, the tongue was deepened in color but did not look like a glossitis. The blood count was normal excepting for a Hb 11.8 and the urine showed a 2-plus albumin,—the leucocytes were normal. Sedimentation rate 28. The X-rays were normal except for a few diverticula in the sigmoid. Ewald test meal displayed an achlorhydria, histidine fast. A series of lumpy masses was present in the upper abdomen. Her skin was yellow-bronze, and she was very weak and hesitant in her actions; her mind, however, was perfectly clear.

Further studies presented normal oral tolerance test and the X-rays a hypermotility of all segments of the small intestine, a prepyloric ulcer, a somewhat shortened esophagus, with herniation of the stomach; several specimens of stool were yellowish-gray and foul smelling, with fat crystals and globules. The analysis of one stool showed in 20 grams 8 grams of neutral and fatty acids. The stool contained a few *B. coli* and a large amount of Gram positive short bacilli, with a number of large phage-like bodies that resembled globs of mucus. These latter may be from the villi of the small intestine, and the bacteria may be important since there were similar bacilli seen also in Case I, and noted in other cases.

This case which is still under observation shows a steady down-hill course in the face of all treatment. The most benefit came from biweekly transfusions of 500 cc of whole blood and a concentrated fluid diet. Nothing availed to control the many bowel movements, the official lead and opium pills every four hours cutting the bowel movements from about 15 to 6 a day. She is still alive.

#### CONCLUSIONS

Two cases are presented that clinically correspond to the description of Whipple's disease or lipodystrophy intestinalis.

This condition seems to be an entity that is diagnosable from the hepaticobiliary and pancreatic conditions in which steatorrhea occurs.

It is suggested that the short Gram positive bacilli (they could not be identified) and the phage-like bodies in the stools may be of diagnostic value in this condition.

The course of the disease is downward in all of the cases described in the literature.

The blood in these cases so far as the anemia is concerned responds promptly to whole blood transfusions and seems to remain high after about six of 500 cc. quantities.

In the classification of chronic diarrheal conditions, this disease should be mentioned.

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## THE EFFECT OF EXCESS SALT INTAKE ON HUMAN BLOOD PRESSURE\*

JOHN McDONOUGH, M. S., AND C. M. WILHELMJ, M. D., Omaha, Nebraska.

IT HAS long been felt that sufficient restriction of sodium chloride intake results in a fall in the blood pressure of both normotensive and hypertensive humans. The following experiment was performed to see the effect of excess salt intake on human blood pressure.

### PROCEDURE

One subject, a healthy normotensive young adult male, was used. Ten blood pressure recordings and four radial pulse determinations were made daily, and the means of these values were taken as the daily blood pressure and heart rate according to the method of Wilhelmj *et al* (1). Body weight was also recorded daily. Since such things as smoking, excitement, exercise, and diet can profoundly affect blood pressure, an effort was made to stabilize these factors. Determinations were always done in the same room at the same time (about one hour before lunch), and following a rest period of at least one-half hour. A mercury sphygmomanometer and auscultation with a stethoscope were used to record blood pressure, and a stopwatch was used in recording the pulse. Smoking was discontinued about one hour before readings

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\*Performed under Grant H1014 National Heart Institute, National Institutes of Health.

were made. The diet was simple and did not vary much from day to day.

Control readings were taken for 23 days, then table salt<sup>1</sup> was taken in the dose range of 25-60 gm/day. Four divided doses mixed in water were taken daily. Salt was taken for 23 days then abruptly discontinued. During the post-salt period, readings were carried out for 25 days.

Plasma volume determinations<sup>2</sup> using the Evan's Blue (T-1824) dye method were done during the salt period and again after the blood pressure and body weight had stabilized in the post-salt period.

### RESULTS

During the 23 days of salt ingestion, 865 gm of salt were taken over and above the salt taken at meals. During the first few days there was a prompt increase in body weight associated with slight but definite swelling of tissues of the face, arms and legs. Pitting edema never occurred. There was a gradual, progressive, highly significant increase in systolic and diastolic pressures. Changes in heart rate were not significant. When salt was discontinued there was a precipitous drop in systolic and diastolic pressures and body weight. These curves then leveled off and assumed

1. Morton's White Crystal Salt. NaCl content 99.53%.

2. Through the generosity of R. E. Lemire, M.D.

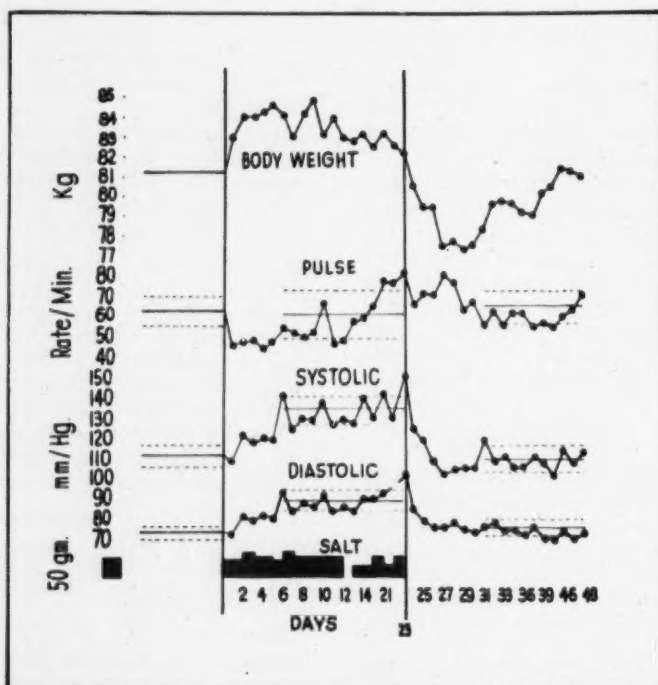


Fig. 1: Broken Lines Represent Standard Deviation from the Mean.



values very close to the values obtained during the control (pre-salt) period (Fig. 1). Plasma volume was slightly but not significantly increased during the salt ingestion (Table I).

TABLE I

## PLASMA VOLUME DETERMINATIONS USING T-1824

	Salt	Post-Salt	Diff
Hematocrit	40.5 mm	44.0 mm	3.5 mm
Total Plasma Volume	4047 cc	3683 cc	364 cc
Total Blood Volume	7085 cc	6851 cc	234 cc

## THE EFFECT OF FEEDING LARGE AMOUNTS OF EMULSIFIERS POLYOXYETHYLENE (20) SORBITAN MONOSTEARATE (TWEEN 60) AND SORBITAN MONOSTEARATE (SPAN 60) TO HUMANS

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**T**HE PARTIAL fatty acid esters of the anhydrides of the sugar alcohol sorbitol and their polyoxyethylene derivatives have found increasing use within the past decade as emulsifying agents in a variety of common commercial foods and in pharmaceutical preparations (1).

The present study was undertaken to evaluate the pharmacological effect of two representative members of this class of emulsifying agents in doses far larger than would be ingested normally through foods or drugs, given for a period of 28 days to relatively large groups of subjects.

## MATERIALS AND METHODS

**A. Materials Tested:** The subjects were given gelatin capsules containing Span 60® (0.5 gram each) or gelatin capsules containing Tween 60® (0.5 gram each), or placebo capsules containing corn oil and resembling the Tween capsules in size, shape, consistency and color. Six capsules of the respective materials were given twice daily (equivalent to 6 grams per day of Tween or Span) for 28 consecutive days.

**B. Subjects Used:** The subjects of this study were patients of a chronic disease and old people's infirmary and hospital personnel pursuing their daily occupations. In this paper they are referred to as "patients" or "normals," respectively. The infirmary patients had been institutionalized for care of a variety of diseases,

From the Hektoen Institute for Medical Research of the Cook County Hospital, Chicago, Illinois and the Oak Forest Infirmary, Oak Forest, Illinois.

Supported by a grant from the Atlas Powder Company, Wilmington, Delaware.

1. Span 60® is the trade mark of Atlas Powder Company, Wilmington, Delaware, for sorbitan monostearate.

2. Tween 60® is the trade mark of Atlas Powder Company, Wilmington, Delaware, for polyoxyethylene (20) sorbitan monostearate.

## DISCUSSION

The effect of massive daily doses of salt in this case was a highly significant elevation in systolic and diastolic blood pressure together with an increase in body weight. When salt was discontinued, blood pressure and body weight promptly fell to low levels and then returned to normal. Since the plasma volume was not appreciably affected by the high salt intake, increased vascular volume was probably not the only factor responsible for the elevation of blood pressure. Cellular edema may have been a factor; and edema of the arterioles resulting in increased total peripheral resistance is certainly a possibility.

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notably cerebral degenerative disease, generalized arteriosclerosis, arthritis, neurologic disorders, or inactive pulmonary tuberculosis. Most were between the ages of 35 and 70 years. Thirty-four patients were fed Tween 60, 32 Span 60 and 25 placebo. The normal subjects were free from disease at the time of study and were between the ages of 25 and 40 years. Ten were fed Tween 60, 10 Span 60 and 10 placebo.

**C. Methods:** The infirmary patients were screened by a complete clinical and laboratory examination to eliminate anyone with active, metabolically significant disease. Laboratory examinations were done before feeding of the test material or placebo was started ("initial"), after 14 days of feeding ("midterm") and at the conclusion of the 28 day program ("final"). These examinations included (1) *urinalysis* for albumin (sulfosalicylic acid method), reducing substances (Clinitest® tablets) and acetone (Acetest® tablets); (2) *hemogram* including hemoglobin content (gm./100 cc.), red blood cell count, white blood cell total and differential count, red cell fragility and hematocrit (determined by standard technics); and (3) a variety of *blood chemical analyses* which are listed in Table I together with the limits of normal accepted in this laboratory.

TABLE I

## TESTS USED IN BLOOD CHEMICAL ANALYSIS (WITH LIMITS OF NORMAL)

- Total serum proteins - 6.0 to 8.0 gm. per 100 cc. (1).
- Serum albumin - above 3.5 gm. per 100 cc. (1).
- Serum globulin - below 3.0 gm. per 100 cc. (1).
- Cephalin-cholesterol flocculation - 0 to 1+ (2).
- Thymol turbidity - below 5 units (3).

3. Ames Company, Elkhart, Indiana.

- Zinc sulfate turbidity - below 12.5 units (4).  
 Phenol turbidity - below 18 units (4).  
 Gamma globulin turbidity - below 1.25 gm. per 100 cc. (5).  
 Total serum bilirubin - 0.3 to 1.2 mg. per 100 cc. (6).  
 Bromsulfophthalein (BSP) - less than 6 percent retention in serum (7).  
 Non-protein nitrogen (NPN) - 20 to 40 mg. per 100 cc.  
 Creatinine - up to 1.5 mg. percent.  
 Blood urea nitrogen (BUN) - 10 to 20 mg. per 100 cc.  
 Total serum cholesterol - 150 to 250 mg. per 100 ml.  
 Percentage of cholesterol esters from total cholesterol above 60 percent (8).

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Initially, 10 patients completed a full course of Tween 60 administration and nine patients were studied during a complete course of Span 60. Because of abnormalities in certain tests during observation, nine additional patients were observed during ingestion of Tween 60, seven during ingestion of Span 60 and nine during ingestion of placebo capsules. In these patients, only those tests which showed abnormalities in the first 19 patients were performed.

To investigate more thoroughly the effect of ingestion of Span 60 or Tween 60 upon the bromsulfophthalein (BSP) retention test, 47 additional patients were studied for BSP retention and urinalysis only (15 ingested Tween 60, 16 Span 60 and 16 placebo capsules) and 30 normals were tested for BSP retention only (10 ingested Tween 60, 10 Span 60 and 10 placebos).

## RESULTS

**Clinical Findings:** No specific complaint was registered and the physical findings remained unchanged in all subjects. In two infirmity patients, mild diarrhea was observed on Tween 60. This stopped spontaneously, without interruption of medication. Two normal persons also developed loose stools after ingestion of Tween 60. They were again given Tween 60, 6 grams per day for 20 days and neither had a recurrence.

**Urinalysis:** Eight of the 34 patients who received Tween 60 had traces of albumin on either the mid-term or final test when the initial urinalysis was free of

albumin. One patient in this group showed 3+ albuminuria in the mid-term test, but none on the final test. Eleven of the 32 patients who received Span 60 and whose urines were albumin-free initially showed a trace of albumin on the mid-term or final test, while two of the 25 patients who received placebo showed albuminuria.

No patient in the placebo group or Tween group developed glycosuria while on medication. Four patients who received Span 60 showed glycosuria in the mid-term or final test. Of these, two refused and two were given a standard glucose tolerance test. One had frank diabetes and the second an abnormal glucose tolerance test, both apparently antedating the study and having been missed during screening. However, to test Span 60 further for a possible glycosuric effect, four non-diabetic patients in the fasting state were each fed 20 grams of Span 60. None showed elevation of the blood sugar in the first four hours after ingestion of the material and none had reducing substance in the urine during the 24 hour periods before and after ingestion of Span 60.

False positive Acetest® reactions were noted when the reaction was carried out in urine specimens collected at the time of the bromsulfophthalein test. It was found that one drop of bromsulfophthalein solution, diluted approximately 1:200, when added to Acetest® reagent produced a strong purple color. In the normals who received bromsulfophthalein, the urines collected shortly after injection of the dye became deep purple when alkalinized. The Acetest® remained negative in the subjects receiving Tween 60 or Span 60, if tested apart from the bromsulfophthalein retention test, except for one patient who was a diabetic and had 4+ glycosuria at that time.

**Hemograms:** There were no significant changes in hemoglobin content, hematocrit, red cell count or red cell fragility in any patient studied. None of the first 19 patients who received Tween 60 showed significant variation in the white cell count. Two of the first 16 patients who received Span 60 had leucocytosis (in one the count returned to normal by the final test) and one had a leucopenia of 3500 WBC/cu. mm. on the final count. One of the first nine patients who received placebo also had a leucopenia of 3500 WBC/cu. mm. on the final count.

**Blood Chemical Analyses:** The first 19 patients who received Tween 60 or Span 60 developed no significant abnormalities in cephalin-cholesterol flocculation, thymol turbidity, zinc sulfate turbidity, serum cholesterol, cholesterol esters, and serum creatinine. Therefore, except for zinc sulfate turbidity, these tests were not done on the subsequent 25 patients given these agents (or placebo) because of the constant normality. Zinc sulfate turbidity was re-tested because of numerous control values above normal which did not vary much during the period of observation. Similarly, phenol turbidity and gamma globulin turbidity were tested in 44 patients. In these, the percentage of abnormal values was of the same order in patients who received placebos as in those who received Span or Tween. One patient who received Tween 60 developed a slight decrease of serum albumin, and one moderate increase of gamma globulin. One patient who received Span 60 had a slightly elevated total serum bilirubin on one deter-

mination which had returned to normal by the next determination. There were no significant differences in serum non-protein nitrogen (NPN) or in blood urea nitrogen in the groups receiving Tween 60, Span 60 or placebo. Table II summarizes the incidence of abnormal findings in these and related biochemical tests.

TABLE II  
SIGNIFICANT CHANGES IN BLOOD CHEMICAL DETERMINATIONS

Test	Tween 60		Span 60		Placebo	
(with border of abnormality considered significant)	No. of tests	No. of significant changes	No. of tests	No. of significant changes	No. of tests	No. of significant changes
Cephalin flocculation (over 2+)	30	0	27	0	0	0
Thymol turbidity (over 5 units)	30	0	27	0	0	0
Zinc sulfate turbidity (5 units above control value)	57	0	48	0	27	1
Phenol turbidity (5 units above control value)	57	(4 pts.) 5	48	(3 pts.) 5	27	2
Serum albumin (reduction below normal and more than 0.5 gm. percent below control value)	30	1	27	0	0	0
Serum globulin (rise above 3 gm. percent and more than 0.5 gm. percent below control value)	30	1	27	0	0	0
Gamma globulin (above 1.25 gm. percent and more than 0.25 gm. percent rise above control value)	57	(6 Pts.) 8	48	2	27	2
BSP (above 6 percent and rise of 3 percent above control value)	See Table III					
Bilirubin (above 1.2 mg. percent with rise greater than 0.5 mg. percent above control value)	30	0	27	1	0	0
Cholesterol (between 125-300 mg. percent and more than 75 mg. percent variation from control value)	30	0	27	0	0	0
Cholesterol esters (below 60 mg. percent and fall of more than 5 mg. percent)	30	0	27	0	0	0
NPN (above 40 mg. percent and rise of 10 mg. percent above control value)	57	2	48	0	27	2

## BUN

(above 20 mg. percent and rise of 5 mg. percent above control value)

57 1 48 1 27 2

## Creatinine

(above 1.5 mg. percent with rise of 0.2 mg. percent above control value)

30 0 27 0 0

## Phospholipids

(8 to 13 mg. percent)

28 0 30 0 32 0

*Bromsulphophthalein Retention:* In a preliminary study without controls, in approximately one-third of the first 35 patients who received Tween 60 or Span 60, BSP retention was abnormal on the mid-term or final test. Only one of the first nine patients who received placebo showed an abnormal result (Table III). In

TABLE III  
RESULTS OF BROMSULFOPHTHALEIN RETENTION TESTS

Group	No. Persons Tested	No. Persons with at Least 1 Normal and 1 Abnormal Result			
		Tween 60	Span 60	Placebo	No Medication
Initial Group of Infirmary Patients	44	8	7	1	..
Second Group of Infirmary Patients	47	1	0	0	..
Hospital Personnel	30	1	0	0	..
Hospital Personnel	2	..	..	..	2

individual patients, the results of BSP retention varied from 3.1 to 13.3 percent, the average variation between results being 5.9 percent. Several of these patients had been included despite initial borderline abnormalities; for example, three patients who received Tween 60 had initial BSP retention of 7.5, 7.0 and 7.0 percent respectively. Furthermore, in two patients who received Tween 60 and in three who received Span 60, the BSP retention, which was normal to begin with, became abnormal at mid-term, but was again normal after completion of the course of medication.

Because of these marked variations in the results of the BSP test, similar patients from the same infirmary population were tested solely for BSP retention while taking Span, Tween or placebo. Fifteen patients received Tween 60, 16 received Span 60 and 16 received placebo according to the same schedule as the previous patients. In order to obtain 47 patients with normal BSP retention to begin with, in this population it was necessary to test 195 patients. Among these patients, one of the 15 who received Tween 60 had an initial BSP retention of 2.8 percent, a mid-term value of 15.0 percent which was 4.0 percent four days later, and a final value of 5.6 percent, which was 4.0 percent four days later. None of the 16 who received



Span 60 and none of the 16 who received placebo showed abnormal BSP retention at any time during observation. None of these 47 patients had an elevated temperature at the time of testing.

To further evaluate the effect of the materials tested on the BSP retention, 30 normal persons received Tween, Span or placebo according to a similar schedule. One person out of 10 who received Tween 60 showed an abnormal BSP retention at mid-term (13.0 percent), but two days later it was normal (1.0 percent) and it was normal at the final test (3.8 percent). The remaining 29 normals had normal BSP retentions on every test.

Two additional normal persons were observed over a two week period *without receiving medication of any sort* and while free of disease. Initially, they had BSP retentions of 3.0 and 2.5 percent but on re-testing two weeks later showed abnormal values of 7.0 and 10.0 percent respectively.

*Miscellaneous:* The serum phospholipids (2) were determined in the second group of 49 infirm patients. No significant change was noted in the levels before or after medication.

#### DISCUSSION

Ingestion of large amounts of Tween 60 or Span 60 daily for one month had no clinically recognizable adverse effect. None of the persons who received these materials or placebos of corn oil showed a significant variation in physical findings. In general, despite the large amounts of these agents taken, subjective tolerance was good. There is no convincing evidence that the isolated instances of diarrhea found are due to the administration of Tween 60 because this symptom disappeared in each case even though medication was not interrupted.

The interpretation of the laboratory findings is complicated by the fact that most of the abnormalities seen were found frequently in the survey before medication was started, appeared frequently in the placebo group as well as in the test groups, and were often found on mid-term examination, but not on the final determination.

The transient albuminuria encountered in some subjects can be considered due to mild renal alterations not uncommonly found in the elderly person. Glycosuria did not appear to be produced by these agents. The frequent positive reaction to the acetone test noticed early in the testing was apparently due to misinterpretation of the Acetest® reaction when BSP contaminated the urine. When this possibility was appreciated and guarded against, acetonuria was not observed. Attention is called to the possibility of misinterpretation of the Acetest® whenever the urine contains a dye which is blue to purple in alkaline medium.

No hematologic abnormalities were encountered from the ingestion of Tween 60 and Span 60 in the doses used during the period of this study.

Of the blood chemical determinations commonly employed to evaluate the function of the major parenchymal organs, the cephalin-cholesterol flocculation, thymol turbidity and the serum levels of proteins, cho-

lesterols and non-protein nitrogenous substances were not significantly altered. Abnormal results in zinc sulfate, gamma globulin and phenol turbidity are not specific for any one disease. The chemical basis of the phenol turbidity test is not clear, but the other two are related to gamma globulin concentration (3). The many abnormal values for these tests did not appear to be caused by the substances ingested since they appeared as often on initial or mid-term determination as on final, and as frequently in those receiving placebo as those receiving Tween 60 or Span 60. No significant change in the serum phospholipids occurred in 15 patients who ingested Tween 60 and in 16 patients who ingested Span 60. This is of interest since sustained hyperlipemia can be induced in rabbits by intravenous injection of surface active agents (namely Tween 80 and Triton A-20) (4, 5). The degree of BSP retention is determined by the competence of hepatic circulation in addition to the capacity of the liver cell to excrete brom-sulphophthalein. Moreover, variations in retention may result from changes in posture, exercise (6, 7) and temperature (8) in the absence of hepato-biliary tract disease. Even if these factors are avoided, significant variations in dye retention may occur when the 5 mg./kg. test is used which have been attributed to entero-hepatic recirculation of the dye (9). Possibly administration of a slightly lesser dose of BSP like 4 mg./kg. may be advisable in studies of this type to avoid the inclusion of borderline alterations of the retention not due to significant and reproducible hepatic changes. In the initial infirm study these factors may have been operative in producing an occasional abnormal BSP retention. But because of the number of abnormal tests in the initial group, further studies were done to eliminate some of the above possible sources of error. The study of the second group of infirm patients showed that no reproducible effect on BSP excretion results from ingestion of Span 60 or Tween 60. This was confirmed in the group of normal personnel. Indeed, in this group two instances of obviously false positive BSP retention occurred. Therefore, no evidence exists that the abnormal BSP retentions noted in the first infirm group can be attributed to the substances given.

#### SUMMARY AND CONCLUSIONS

1. To evaluate the pharmacologic effect of emulsifying agents commonly used in commercial foods, a group of patients of an old people's and chronic disease infirmity were fed daily for 28 days large amounts (6 grams) of Tween 60 and Span 60. Nineteen patients were given Tween 60 (polvoxyethylene [20] sorbitan monostearate), 16 were given Span 60 (sorbitan monostearate) and 9 were given corn oil placebos in capsules resembling the Tween 60 capsules. Each patient was followed clinically and by many laboratory tests.

2. No untoward clinical reactions were encountered. No significant changes occurred in the following tests: cephalin-cholesterol flocculation, thymol turbidity, serum albumin, globulin, bilirubin, cholesterol, cholesterol esters, creatinine, non-protein nitrogen, phospholipids, and blood urea nitrogen. Urinalyses and hemograms were not significantly changed.

3. Significant variation in the zinc sulfate, phenol

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and gamma globulin turbidity tests occurred without apparent cause in a number of patients tested. Caution is recommended in the interpretation of a single abnormal result in one of these tests.

4. Because of the finding that several BSP tests in the initial group of infirm patients varied from normal to abnormal, these substances were fed to another group of patients from the same infirmary (15 Tween 60, 16 Span 60 and 16 placebo) and to normal hospital personnel (10 Tween 60, 10 Span 60 and 10 placebo). In these patients and in the normals variations in BSP tests were not observed to like degree; in only one instance did an abnormal test follow a normal one during observation. At the same time in two normals who received no medication BSP tests varied from normal to abnormal in the space of two weeks. Because the abnormalities were not reproducible in a second group of patients and in normals, the variations found in the BSP test in the first group of patients are believed to be false positive reactions not related to the substances ingested.

5. The nitroprusside reaction for acetonuria may be misinterpreted whenever the urine contains a dye (such as bromsulphophthalein) which gives a purple or blue color in an alkaline medium.

6. The methods used in this study produced no evidence that the feeding of 6 grams of Span 60 or Tween 60 daily for 28 days produces deleterious effects to humans.

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## LATERAL DOUBLE CONTRAST BARIUM ENEMA EXPOSURE FOR RECTAL LESIONS

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RECTAL lesions have often been a source of embarrassment to the roentgenologist. Large lesions are often undetected because of the considerable distension of the rectal ampulla, looping of the sigmoid, and the considerable ileo-cecal incompetency that often occurs.

Even though this area of the colon properly belongs to the proctologist, as long as requests for examination come to the radiologist it behooves him to examine this area as thoroughly as possible. To partially overcome the difficulties, routine spot filming and radiography of the recto-sigmoid in the left lateral projection has been undertaken during the filling of the colon under fluoroscopic control. Although this procedure may reveal sigmoid lesions which may be obscured at a later date when the entire colon is filled, nevertheless, multiple abnormalities of the rectum are often missed.

Post evacuation studies in the PA and lateral projections are of great assistance. In order to improve the post-evacuation exposures a heaping teaspoon of tannic acid is added to three pints of barium mixture. Unfortunately, the frequent redundancy of the sigmoid loops and the presence of barium filled ileal loops often obscures the detail of the examination.

Levene and Veale have presented a special spray  
JULY, 1954

technique to illustrate rectal lesions by partial filling of the recto-sigmoid by means of a spray.

Raap, and recently, Moreton have described the "sitting position" for obscure rectal lesions. This employs the double contrast (barium and air) technique with the exposure taken in the sitting position.

The simple double contrast exposure in the lateral projection, however, yields excellent results, is easier to perform, and requires little additional time. It is used as a routine procedure because of its simplicity and has yielded excellent results.

The rectum and distal sigmoid are visualized in fine detail. The normal anatomical structures of the rectum stand out in bold relief, and it is possible to pick up lesions that are quite small in size.

Even large lesions, when sessile, are at times quite difficult to pick up in the routine barium enema. With this procedure it is easy to demonstrate such lesions since both the anterior and posterior walls are thrown into distinct relief.

On occasion, rectal lesions result in insufficient evacuation. This technique may therefore be slightly modified, using the translateral exposure with the patient either prone or supine, depending on whether the anterior or posterior wall of the rectum is to be visualized. (Figure 4).



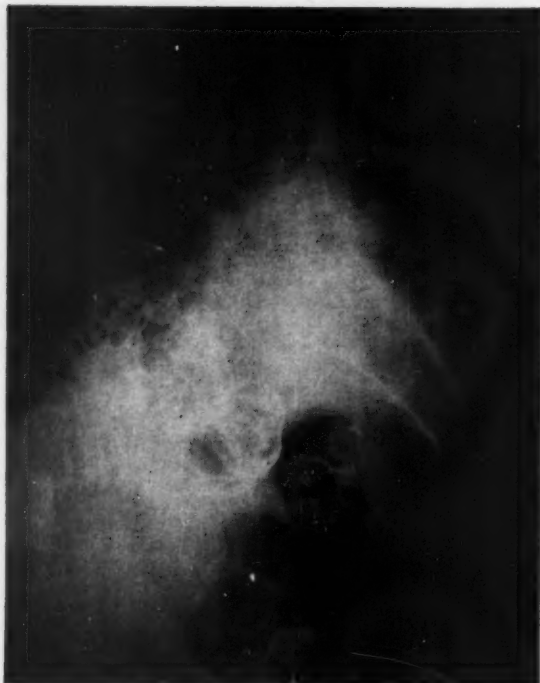


Fig. 1: A large sessile neoplasm (adenocarcinoma) on the posterior wall of the rectum. This was not evident on the routine films. Multiple ileal loops prevented its demonstration in the post-evacuation and postero-anterior double contrast exposures. The lateral double contrast exposure clearly outlines the lesion in its entirety.



Fig. 2: Small rectal polyp on the anterior wall of the rectum.



Fig. 3 (retouched): Small rectal polyp on the posterior wall of the rectum.



Fig. 4 (retouched): Two double contrast barium enemas failed to reveal any lesion, because of the patient's inability to evacuate completely. The translateral exposure with the patient prone illustrated the entire extent of a posterior wall sessile lesion, corroborated at operation (adenocarcinoma). The dotted lines indicate the extent of the lesion.

This simple technique in no way competes with the proctoscope. What is presented is a simple addition to the routine barium enema examination as a worthwhile refinement.

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## COMPRESSION MUCOSAL STUDIES WITH A PNEUMATIC PADDLE

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THE PRE-EMINENT role of compression mucosal studies has been firmly established in recent years. Radiologists and gastroenterologists alike make every attempt to demonstrate a niche. In this connection, compression spot filming has played the predominant role. To achieve this end, the manufacturers have improved their various spot film devices and have installed rotating anode tubes under the table.

There are certain difficulties that routine spot filming has to overcome. In the upright posture both voluntary and involuntary motion is more difficult to control than in the horizontal posture. Compression is also more difficult in the upright than in the relaxed horizontal posture. The smaller the area of the spot exposure, the greater must the penetration be if the time exposure is to be kept sufficiently short to obviate peristaltic motion. The stationary grid requires increased exposure, but still is inferior to the Potter-Bucky diaphragm.

In other words, compression mucosal studies performed in the horizontal position would afford the advantages of greater relaxation of the patient, the Potter-Bucky diaphragm, narrow cone, and increased focal distance.

Different compression techniques have been devised in the horizontal posture to supplement spot filming. One of the finest compression devices has been designed by Franklin X-Ray Corporation. This consists of a paddle with a metal ring at one end to localize the suspected area in the center of the circle under fluoroscopic control. Graded compression by a pneumatic pump can then be made under the fluoroscope to be certain that the correct degree of compression is obtained for best visualization of the desired area. The patient is relaxed and a great degree of compression is obtainable, even indirectly in inaccessible areas. As a matter of fact, over-compression is very simple indeed, and must be guarded against. With experience, the correct amount of compression is readily obtained to best demonstrate the lesion.

With the use of this paddle and the Potter-Bucky diaphragm, fine detailed radiograms can be obtained even with obese patients and ordinary stationary anode tubes. The paddle is especially valuable in bleeding patients or any others who are unable to stand during an examination. A mild degree of compression can be carefully applied to the bleeding patient with no untoward danger.

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Fig. 1A and B: Frontal and lateral views of the pneumatic compression paddle, with the balloon partially inflated.



Fig. II A



Fig. II C

Fig 2A, B, C, D and E: A hypersthenic heavy set patient, who for several years had attacks of melena periodically with no associated gastro-intestinal symptoms. He had been examined repeatedly by radiologists of note without demonstrating a niche. This examination was conducted shortly after his bleeding had stopped. The routine films failed to reveal any niche (A and B). Figure C represents a spot film in the upright using 90 KV, 200 ma,  $\frac{1}{4}$  second exposure, and a cassette with an incorporated lysholm grid.

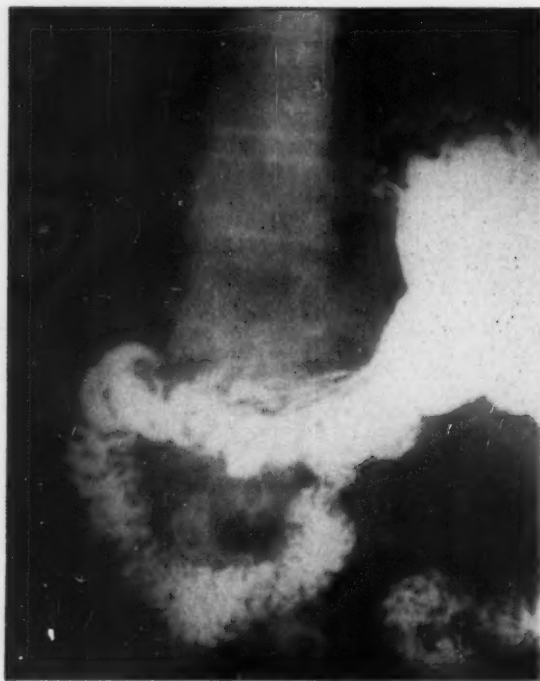


Fig. II B

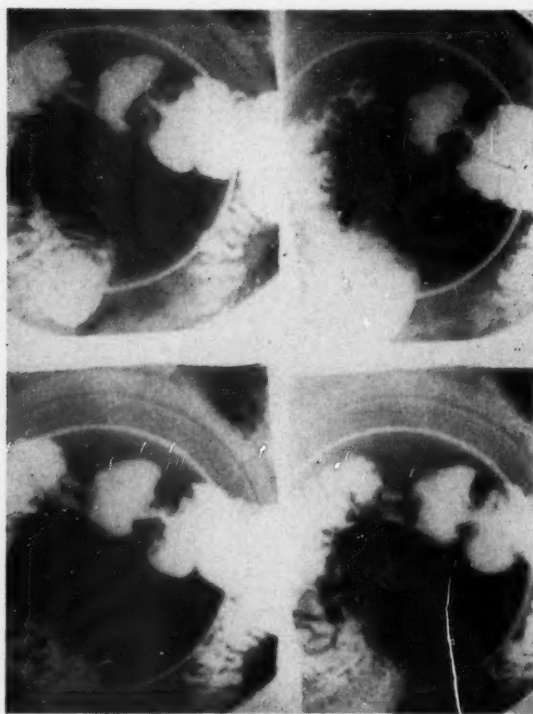


Fig. II D

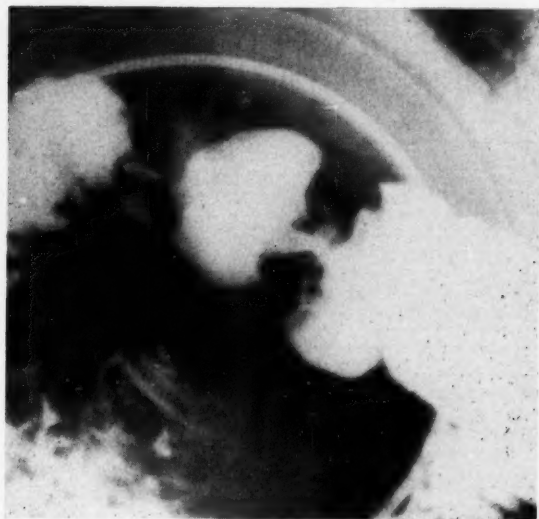


Fig. II E

Figure D represents a polygram taken with the compression paddle. One of these squares is illustrated in E. The ulcer is clearly demonstrated, including the entire ulcerated area down to the base with the edematous walls represented as an area of filling defect.

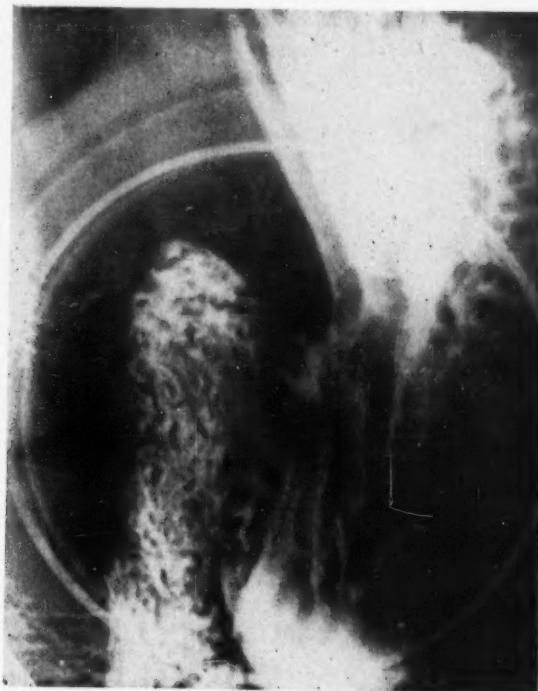


Fig. III B



Fig. III A

Fig. 3A, B: A patient with a gastric ulcer who did not improve on medical therapy. A and B are quarters of polygram without and with compression. The rugae radiate to the ulcer indicating its benign character. The true size of the ulcer is better demonstrated with compression. The operative specimen showed the ulcer to be benign.

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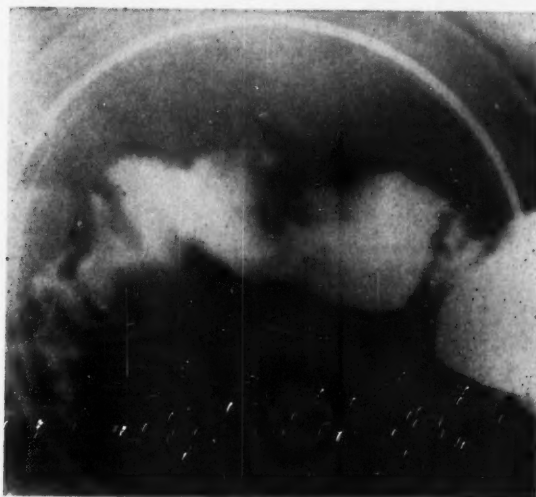


Fig. IV A

Fig. 4A, B, C: Three examples of duodenal ulcer. A quarter of a polygram is presented in each case.

A. A hypersthenic stocky physician, 220 lbs., five feet seven inches tall. None of the routine films illustrated any duodenal defect. Because of the size of the patient, upright compression spot filming was dispensed with and the pneumatic compression paddle substituted. The central crater is clearly demonstrated.





Fig. IV B

B. Illustration of a central niche with pseudodiverticulum formation on the greater curvature side. Note the detail in this radiograph, taken in this case with an ordinary stationary anode tube.



Fig. IV C

C. This case presents a large central ulcer crater on compression with small static flecks in the adjacent mucosa. The compression was released and then re-applied, again demonstrating these static flecks. A diagnosis of a large duodenal ulcer with smaller kissing ulcers was therefore justified.



Fig. V

Fig. 5: This patient had been examined elsewhere radiographically a short time earlier and diagnosis of duodenal ulcer had been made. Only with the demonstration of a normal rugal pattern, was the physician convinced that the duodenum was normal. Although the patient's symptoms suggested a hiatus hernia, this could not be demonstrated by routine procedures. With the use of the pneumatic compression paddle, the small sliding hiatus hernia shown in the figure was finally revealed.

Conclusion: A compression paddle is presented which is considered to be an important addition to the radiologist's and the gastro-enterologist's armamentarium. It is especially valuable if the finest spot film device is not available. Even where it is present, this device is useful with obese or hypersthenic patients. It is of considerable help with patients who are bleeding or cannot stand for any reason whatsoever.

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## ON THE MECHANISM OF ULCER PAIN

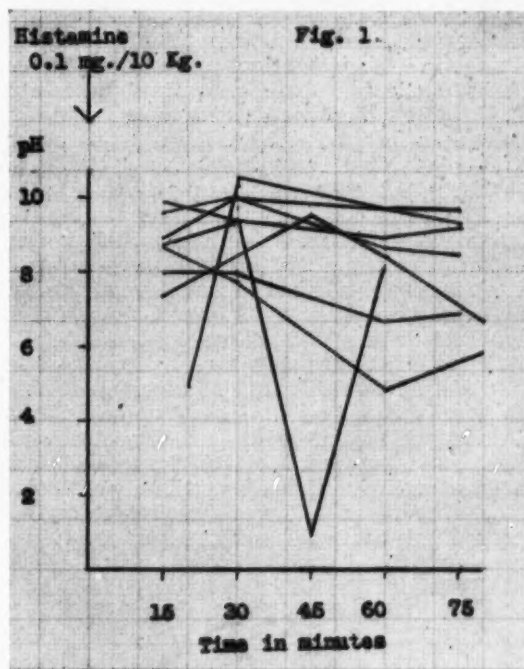
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THE CAUSE of peptic ulcer pain still remains to be explained. The view that the pain is due to direct chemical irritation of the ulcer by hydrochloric acid has been strongly supported especially by Palmer (12, 13, 14). He is of the opinion that hydrochloric acid produces pain in patients with peptic ulcer so invariably that the introduction of 0.1 N HCl into the stomach may be used as a diagnostic test. Bönninger, in 1908, was probably the first to suggest this "acid test." Palmer's studies supporting the "acid theory" are too well known to require further explanation, and the same is true of the theoretic objections made against his opinion. The incidence of positive "acid tests" varies greatly in different materials. Palmer himself obtained positive results with this test in 97 per cent of a series of 314 patients with peptic ulcer, Hardy in 78 per cent of 77 patients, and Bonney and Pickering in 19 patients in a series of 22 patients (15). According to certain other workers the incidence of positive results is lower. Thus Ruffin et al., in a series of 100 patients with peptic ulcer, obtained a positive test in 37 per cent only (16) and Gottsegen and Hermann in 42 per cent of 121 cases (9). Cavallini et al. reached a fully negative conclusion regarding the diagnostic significance of the "acid test" (7). The author's own experiences with the "acid test," although limited, are also negative. In a study carried out with Bundul on the gastric motility during epigastric pain, attempts were made to produce pain in 15 patients with peptic ulcer by the administration of 200-300 cc. of 0.1 N HCl but the result was negative. The mental tension caused by the x-ray examination may have contributed to this.

The measures by which the acidity of the gastric content is altered by the addition of either acids or alkalis also influence gastric and duodenal motility. Of the most commonly used antacids, sodium bicarbonate especially increases gastric peristalsis distinctly (3). This motility effect of sodium bicarbonate as well as its relieving effect on gastric distress is independent of gastric acidity (2). Indeed, it is probable that the therapeutic benefit from sodium bicarbonate and other antacids in gastric distress is a result of their effect on motility and not of their neutralizing property (3). Hydrochloric acid also has a characteristic influence on gastric and duodenal motility (e.g., 3, 4). In order that we may evaluate the effect on ulcer pain of each of these variables, acidity and motility, we should endeavor to maintain one of them constant during the test. By following this principle and maintaining the acidity of the gastric content unchanged, Ruffin et al. were able to establish a correlation between ulcer pain and gastric motility (16).

The object of this report was to study the correlation of ulcer pain and gastric acidity under conditions that were as physiological as possible. For this purpose the gastric content was not rendered acid by the

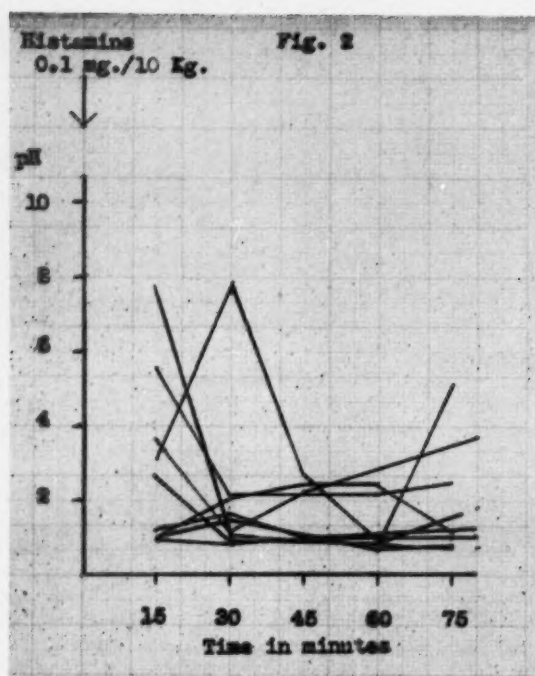
introduction of hydrochloric acid but by the stimulation of acid gastric secretion with histamine. Observations were made of the effect of a subcutaneous histamine injection with and without simultaneous neutralization of the histamine stimulated acid secretion. For neutralization of the acid secretion the patients were given neutralizing toffee to be sucked continuously during the test (® "Antihappo," Pharmaceutical Manufacturers Leiras Oy, Turku). According to the manufacturers' statement, this toffee contains 0.25 Gm. of calcium silicate, 0.12 m. of magnesium oxide, 0.03 Gm. of magnesium carbonate, 0.12 Gm. of calcium carbonate, 1.00 Gm. of milk powder, and 1.79 Gm. of sucrose. The neutralizing power of one piece is equal to 94 ml. of 0.1 N HCl. As first demonstrated by Douthwaite and Shaw (8), and confirmed by Koskinen with "Antihappo" toffee (11), neutralization is more effective if the test subject sucks the antacid preparation slowly rather than swallows it intact. It may also be assumed that the effect of the antacid on gastric motility is considerably smaller when it reaches the stomach gradually. In order to provide similar test conditions during the control test the patients were given toffee similar in appearance and taste but without neutralizing effect. Figs. 1 and 2 show the gastric acidity following histamine injection when test subjects with hypersecretion are given alkaline and ordinary toffee.



Gastric acidity after histamine in test subjects receiving simultaneously alkaline toffee.

From the Medical Clinic of the University, Turku, Finland.

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Gastric acidity after histamine in test subjects receiving simultaneously ordinary toffee.

Histamine stimulated acid secretion can thus be neutralized and even the gastric content rendered alkaline with alkaline toffee. The sucking of ordinary toffee has very little effect on the acidity. The difference in gastric acidity between the two groups is so evident that one would expect, if direct irritation by hydrochloric acid were actually the cause of ulcer pain, that the histamine injection would produce pain only in tests during which ordinary toffee is ingested.

The test series comprised 18 patients with gastric ulcer and 22 patients with duodenal ulcer. The diagnosis had been established roentgenologically in all cases, and in some cases it was later confirmed at operation. The tests were carried out before treatment and before disappearance of the spontaneous pain felt by the patient. On consecutive mornings the patients were given 0.1 mg. of histamine per 10 kg. of body weight, after which they continuously sucked a piece of alkaline or ordinary toffee. The tests were started alternatively with each toffee.

In 32 cases the histamine produced no pain in either test. Five patients, three of whom had duodenal ulcer, complained of pain after histamine in the placebo test but not when given alkaline toffee. The pain started usually about half an hour after the injection and was considerably less severe than the patient's usual ulcer pain. Three patients, including two with duodenal ulcer, felt post-histamine pain when given alkaline toffee but not when given ordinary toffee. One of these patients reported rather severe and the other two milder pain.

#### DISCUSSION

The results obtained in these tests indicate that

histamine relatively rarely causes pain in patients with peptic ulcer and that the pain, when present, is usually considerably less severe than that ordinarily felt by these patients. No distinct difference was noted in the occurrence of the pain when the histamine stimulated acid secretion was or was not neutralized. Should the direct chemical irritation of hydrochloric acid play a decisive part in the mechanism of ulcer pain it would be difficult to understand these results. This study therefore seems to be additional evidence against the "acid theory."

#### SUMMARY

The writer has observed the effect of histamine injection on ulcer pain in patients with an active peptic ulcer when the histamine stimulated acid secretion was or was not simultaneously neutralized. In a series of 40 patients, histamine produced pain in 8 patients only. The pain was usually considerably less severe than the ulcer pain ordinarily felt by these patients. The neutralization or non-neutralization of the acid secretion had no distinct influence on the occurrence of the pain. In the writer's opinion these test results are additional evidence against the "acid theory" of ulcer pain.

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## THE EFFECT OF VARIATIONS OF POSITION UPON THE GASTRO-DUODENAL ARTERIAL PRESSURE

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MANY PAPERS have appeared in recent years discussing the management of massive upper gastrointestinal hemorrhage. These may be grouped into three methods of treatment. The first method (1, 2) considers all these cases of massive hemorrhage as surgical emergencies. The only question being what constituted a massive hemorrhage. They consider this to be bleeding with such speed that replacement with adequate amounts of blood cannot restore the blood volume and in which the patient presents a picture of shock. Immediate gastric resection and removal of the ulcer is advised. There are those (3) who go so far as to say that even when no ulcer can be demonstrated at surgery, that a blind gastric resection should be performed. The second method of treatment (4, 5, 6) treats all patients conservatively with adequate blood, bed rest, antacid, and either the Meulengracht or Andresen diet. These writers claim to have reduced the mortality rate from the massively bleeding ulcerative lesions to approximately 4% or 5%. When it is considered that in previous years the mortality rate was as high as 25%, this is a great reduction. The third method (7, 8, 9) takes an intermediary course. This group is of the opinion that probably 95% of massively bleeding cases can be controlled well with adequate replacement of blood, an antacid to keep the gastric acidity about pH 3.5, and the use of Gelfoam and thrombin. The amount of blood given may be as high as ten thousand cubic centimeters in a twenty-four hour period. The Gelfoam and thrombin produces a thrombus at the site of bleeding. By the use of this technique of applying a hemostatic agent to the site of the bleeding, the group has managed to reduce the overall mortality to 3.3% in a series of 120 patients so treated. This group definitely states, however, that there is a small percentage of patients in whom emergency surgery would be indicated. This accounts for 5% of the patients or less. In these it is possible that the use of the hemostatic agent and the replacement of blood would fail because of the sclerotic character or the size of the bleeding vessel.

In reviewing the statistical analyses of all authors, it is evident that bleeding gastric ulcers constitute a relatively small percentage of the cases. Seventy percent of all bleeding from the upper gastrointestinal tract is the result of duodenal ulcers. Of this 70% of ulcerative lesions of the duodenum which bleed, the preponderately vast majority are posterior wall ulcers which have penetrated into the pancreas. In these the bleeding is the result of erosion into the gastroduodenal artery or a branch thereof. Heretofore all studies in the management of massive upper gastroduodenal hemorrhage have been conducted along clinical lines. The emphasis has been placed upon the proper selection of cases for surgery or those patients which could best be treated medically. There has been no laboratory ap-

proach to the problem in an effort to determine what, if anything else, could be done to further reduce the number of patients coming to surgery or to clearly define which cases should go to surgery and which ones should be treated medically.

The first laboratory approach to the problem was the paper by LeVeen, Mulder, and Prokop (10) entitled, "The Physiological Mechanism for Death in Massively Bleeding Peptic Ulcer." They approached the problem in the laboratory and attempted to determine the effects of massive femoral artery bleeding as compared with massive bleeding from the gastroduodenal artery. They demonstrated that massive hemorrhage arising from the gastroduodenal artery selectively reduced the hepatic artery blood pressure and blood flow far in excess of that produced by hemorrhage from the femoral artery. This selective reduction of blood flow became greatest when the systemic blood pressure reached levels below 100 mm. of mercury. In hemorrhage there was shown to be a reduction in the oxygen tension of the portal venous blood which makes oxygen from this source unavailable in normal amounts to the liver. According to Blalock (11) even moderate hemorrhage reduces the portal blood flow by more than half. In addition, the resistance which the liver offers to the flow of blood increases after hemorrhage and by so doing further decreases the oxygen tension and as a result hypoxia in the liver increases. A selective hepatic anoxia results which can be offered as the possible significant physiological basis for the mechanism of death due to bleeding from the gastroduodenal artery as a result of an erosive duodenal ulcer. The deterioration of the hepatic function is progressive and with continued anoxia a point of irreversible change is reached. The authors therefore believe it fairly logical that urgent surgery be performed to stop the bleeding.

The authors' experience (12) in the management of one hundred and forty-eight cases of massive upper gastrointestinal hemorrhage, however, does not quite support this contention. In this series of patients treated conservatively the mortality rate of 1.7% would seem to indicate that this serious liver anoxia is more theoretical than real. These were all patients in whom the red blood count was less than three million and who were in moderate or severe shock as a result of the speed of blood loss.

The physiological studies by Leveen, Mulder, and Prokop are important in calling attention to what might occur in these massively bleeding cases. It points the way toward a laboratory approach to the problem. With this in mind, the authors attempted to apply the laws of physics to the study of the hydrodynamic pressure within the gastroduodenal artery. If the pressure in the gastroduodenal artery could selectively be reduced without impairing in any way the pressure within the hepatic artery, then this reduction in pressure would

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Fig. 1: Note the variation in angle between gastroduodenal and hepatic artery.



have a beneficial effect upon the cessation of bleeding from an ulcerative lesion which had eroded the gastroduodenal artery or its branch. The lower tension within this vessel would permit the hemostatic agent applied to the ulcer crater to better control the bleeding. In addition, we wished to determine whether any changes in pressure within the gastroduodenal artery would directly effect the flow of fluid through the hepatic artery. If a selective reduction of pressure in the gastroduodenal artery could be obtained without affecting the flow through the hepatic artery, then the vitiating effect of anoxia of the liver cells would not occur.

#### METHOD

Twenty-five autopsies were performed. The hepatic, the gastroduodenal, the common hepatic, and the right and left hepatic arteries were dissected out. Drawings were made of the point of origin of the gastroduodenal artery from the hepatic artery and the angle at which this union took place (see Fig. 1). The caliber of the hepatic artery and that of the gastroduodenal artery was then measured (see Fig. 1A).

The importance of noting and measuring the angle of junction of the gastroduodenal artery and the hepatic artery was to determine whether the Bernoulli Effect might occur at the mouth of the gastroduodenal artery by blood in the hepatic artery rushing over it. If a Bernoulli Effect could be demonstrated, then with an increase in the rate of flow of blood through the hepatic artery there should be a decrease in the pressure within the gastroduodenal artery. The measure-



Fig. 1 A

ment of the caliber of the gastroduodenal artery and the hepatic artery is of great importance because of the application of Pouissie's Law. Groat's (13) application of this law to blood vessels demonstrated that the rate of flow was proportional to the square of the diameter. It should be apparent from this that the rate of flow of fluid through a tube 2 mm. in diameter would be four times that in a tube 1 mm. in diameter.

In these twenty-five dissections, a great variation in the angle between the gastroduodenal and hepatic arteries was noted. These can be seen in Fig. 1. There was a considerable variation also in the size of the gastroduodenal and hepatic arteries as noted in Fig. 1A. A replica of the anatomy of the point of union of the gastroduodenal and hepatic arteries was then constructed of glass tubing and the relative calibers of the gastroduodenal and hepatic arteries maintained. Fig. 3 demonstrates one of the glass models constructed representing the hepatic artery, the gastroduodenal artery, and the common hepatic artery. The gastroduodenal artery was then connected to a water manometer indicating positive and negative pressures as shown in Fig. 3.

Water under constant pressure was then run through the hepatic artery and the effect of changes in position

of the gastroduodenal artery were noted in the water manometer connected to this artery. Figures 5, 6, and 7 demonstrate the changes that take place in the pressure within the gastroduodenal artery with changes in position. It can be noted that if the patient is put in the Trendelenberg position and turned on the right side as seen in Fig. 5, that all of the water runs through the hepatic artery freely and that the pressure within the gastroduodenal artery falls off sharply. When the patient is put in a position flat on his back, a positive pressure appears in the gastroduodenal artery. The same increase in pressure is noted with the gastroduodenal artery pointing downward such as would occur with the patient sitting up or standing. In every instance, regardless of the relative caliber of the vessels, whenever the gastroduodenal artery was directed uphill from its origin at the hepatic such as occurs in the high Trendelenberg position, a definite drop in pressure appeared in the gastroduodenal artery. In those vessels in which the hepatic artery was three or more times the size of the gastroduodenal artery, in addition to the effect of gravity in reducing the pressure within the gastroduodenal artery, a definite turbulence effect was exerted at the mouth of the gastroduodenal artery where it joined the hepatic. The re-



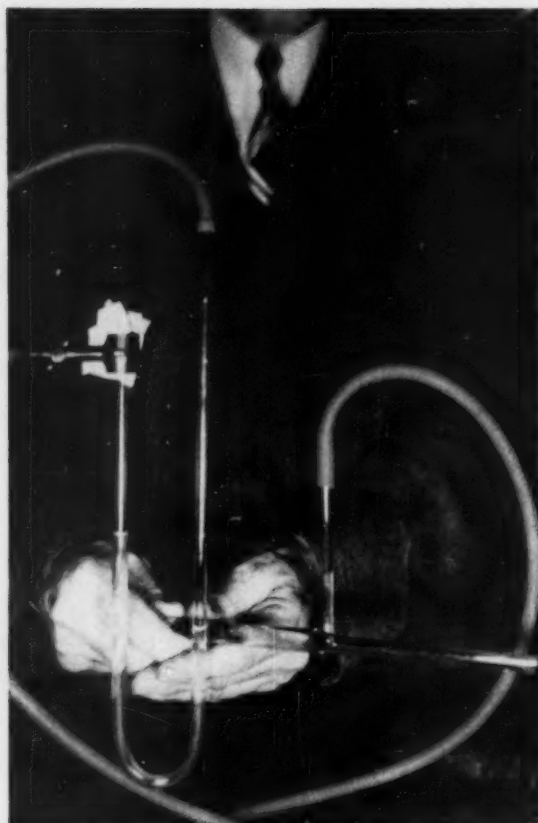


Fig. 3: Glass tubing constructed with gastroduodenal common hepatic, and main hepatic trunk arteries in same relative proportions as noted by dissections in figure 2. Gastroduodenal limb connected to water manometer measuring positive and negative pressure.

sult of this turbulence effect was a further decrease in the pressure within the gastroduodenal artery. A true Bernoulli effect was not obtainable in any of the experiments because in no case was the caliber of the gastroduodenal artery so small in proportion to the hepatic that the true Bernoulli effect could be obtained. In order to obtain the true Bernoulli effect, a marked increase in the rate of flow of fluid through the hepatic artery is required and a marked disproportion between the size of the hepatic and the gastroduodenal artery. The gastroduodenal artery would be considerably reduced far below that possible in a human. For this reason, it can be stated with a reasonable degree of assurance that the Bernoulli effect plays no part whatsoever in the reduction of pressure within the gastroduodenal artery. The falling off of pressure demonstrates in vitro solely the result of the effects of gravity as well as the turbulence effect at the mouth of the gastroduodenal artery where it joined the hepatic.

The experiments were repeated many times and on every occasion this drop in pressure within the gastroduodenal artery was obtained with a change of position in which the patient would be put on the right side and the foot of the bed elevated. In this position, the gastroduodenal artery points uphill and the hepatic artery points downhill. As a result, the blood rushes

Cadaver	Age	Sex	Height	Weight	Gastroduodenal Artery Diam.	Hepatic Art. Diam.
No. 6523	4 mo.	F.	2' 6"	14 lb.	4 mm.	8 mm.
No. 6340	83 yr.	F.	4' 10"	115 lb.	4½ mm.	7 mm.
No. 6347	40 yr.	M.	5'	150 lb.	5 mm.	6 mm.
No. 6343	20 yr.	F.	5' 2"	120 lb.	1½ mm.	6 mm.
No. 5886	54 yr.	M.	5' 4"	155 lb.	4½ mm.	7 mm.
No. 5887	70 yr.	M.	5' 7"	165 lb.	4 mm.	7 mm.
No. 5830	68 yr.	M.	5' 7"	160 lb.	2½ mm.	4½ mm.
No. 5825	60 yr.	M.	5' 7"	150 lb.	3 mm.	8 mm.
No. 5546	67 yr.	M.	5' 8"	150 lb.	2.5 mm.	5 mm.
No. 5540	56 yr.	M.	5' 9"	175 lb.	4½ mm.	6 mm.
No. 5547	60 yr.	M.	5' 9"	150 lb.	2 mm.	5 mm.
No. 5535	53 yr.	M.	5' 9"	190 lb.	3 mm.	6 mm.
No. 5596	42 yr.	M.	5' 9½"	175 lb.	2 mm.	5 mm.
No. 5400	52 yr.	M.	5' 9"	210 lb.	3 mm.	7 mm.
No. 5402	41 yr.	M.	5' 9"	235 lb.	2.5 mm.	6 mm.
No. 5455	62 yr.	M.	6' 1"	240 lb.	2 mm.	6 mm.
No. 5304	60 yr.	M.	5' 11"	240 lb.	4 mm.	8 mm.
No. 5314	45 yr.	M.	6' 1"	185 lb.	3½ mm.	8 mm.
No. 5300	62 yr.	F.	5' 6"	130 lb.	1½ mm.	6 mm.
No. 6234	24 yr.	F.	5' 7"	120 lb.	4½ mm.	8 mm.
No. 5233	33 yr.	M.	5' 6"	165 lb.	3 mm.	7 mm.
No. 5104	56 yr.	M.	5' 7"	190 lb.	2 mm.	5 mm.
No. 5094	36 yr.	M.	5' 7"	170 lb.	2½ mm.	6 mm.
No. 5093	62 yr.	M.	5' 8"	185 lb.	4½ mm.	9 mm.
No. 5096	26 yr.	M.	5' 8"	190 lb.	2 mm.	5 mm.

Fig. 2: Dissection of twenty-five fresh cadavers. Note variations in diameters of gastroduodenal and hepatic arteries.



Fig. 5: With patient in Trendelenburg position the gastroduodenal artery will be in this position as shown by glass model.

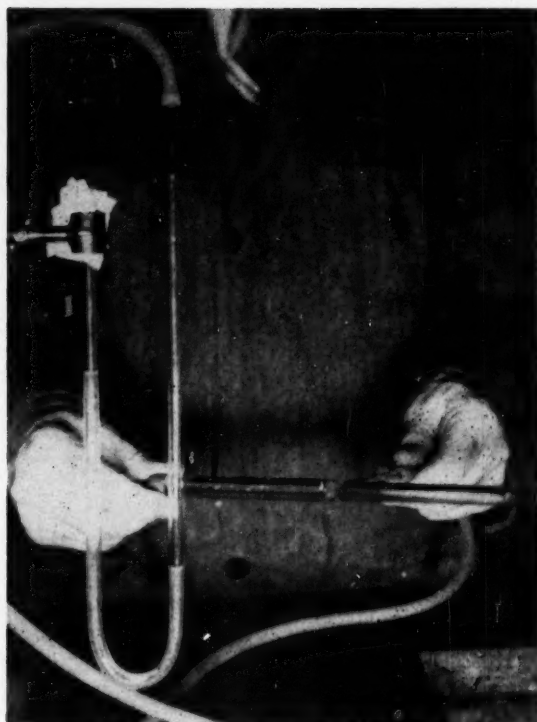


Fig. 6: With patient flat on his back, the gastroduodenal artery would be in position as shown by glass model in this figure.



Fig. 7: With patient in the erect or sitting position, the gastroduodenal artery would be in the position as shown by this glass model.

through the hepatic artery and there is a definite decrease in the intra-arterial pressure in the gastroduodenal artery. The advantage of this position should be apparent. If one had an ulcerative lesion on the posterior wall of the duodenum which had eroded through the gastroduodenal artery and the patient were treated conservatively with adequate blood replacement, Gelfoam and thrombin applied to the site of the bleeding by being fed orally, and if the pressure within the gastroduodenal artery could be selectively reduced so that the clot produced by the Gelfoam and thrombin would stay in position and would not be thrown off by the spurting artery, then it would seem that many cases might be benefited by this additional maneuver. It is suggested that the application of the laws of physics in the management of gastroduodenal hemorrhage might be of some value particularly if a selective decrease in intra-arterial gastroduodenal pressure could be obtained by so doing.

In vitro experiments in which glass tubing is substituted for living tissue which has the ability to contract and go into spasm is open to the criticism that such conditions do not obtain in the living patient. It is generally agreed that those individuals in whom gastroduodenal hemorrhage of a massive type is apt to result in serious consequences generally are found in the older age groups in whom sclerotic vessels are found. A sclerotic artery the mouth of which is fixed in an indurated ulcer is an extremely difficult problem. The authors suggest that such sclerotic vessels in these older age groups are rather comparable to the glass

tubing in the in vitro experiments in that both sclerotic fixed arteries and glass tubing have no power of contraction and have little or no resiliency.

#### SUMMARY

In an attempt to determine what effect changes in position would have upon the gastroduodenal arterial pressure, the authors constructed of glass tubing a replica of the hepatic artery, the gastroduodenal artery, and the common hepatic artery. These were constructed in the same proportions and reproducing the same angle of union between the gastroduodenal and hepatic arteries that were demonstrated at autopsy in twenty-five cadavers. By attaching a water manometer to the gastroduodenal artery and passing water through the hepatic artery under a fixed pressure, it was seen that the patient in the Trendelenburg position and turned on the right side, showed a decrease in pressure in the gastroduodenal artery. This reduction in pressure in the gastroduodenal artery would be of value in the management of penetrating duodenal ulcers with hemorrhage. It is suggested that the reduced gastroduodenal pressure would render the use of Gelfoam and thrombin more effective as hemostatic agents in the control of bleeding duodenal ulcers.

The above observations were applied clinically to six patients in the past six months with dramatic cessation of the bleeding.

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## A METHOD FOR THE RAPID DIFFERENTIATION OF ENTEROBACTERIACEAE

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**R**APID identification of enteric pathogens is desirable so that outbreaks of shigellosis and salmonellosis may be quickly recognized and controlled. Present procedures require 3 to 4 days and consist usually of plating the stool to S.S., MacConkey's or E.M.B. agar plates; the use of enrichment media as Selenite-F and/or tetrathionate broth; fishing colonies from the plates to Kligler's or Hajna's media; and, the next day, inoculation of tubes of fermentable substances. Even if rapid indole and urea tests are employed, and the surface growth on Kligler's or Hajna's medium utilized for agglutination tests, a preliminary diagnosis cannot be issued sooner than about 48 hours after the colonies were fished from the plates. The purpose of this study was to find a method suitable for use in small laboratories and under field conditions, which would permit a faster preliminary identification.

Shorter procedures have been previously described. Bertacchini (1) suggested the first micromethods, permitting observation of the action of isolated organisms on fermentable substances within 4 to 6 hours. This technic, and its further elaborations by Weaver et al (2, 3, 4), have some disadvantages, the most important being the need of a large inoculum for each test substrate. Since the colonies grown on the usual diagnostic plates (S.S. agar, E.M.B. medium, MacConkey plate, etc.) are relatively small, this procedure does not readily adapt to rapid enteric work.

The second approach uses a screening fluid, such as a lactose and/or sucrose broth, or liquid urea medium, into which the colonies are picked from the original plates. After the lactose-sucrose broth has been incubated for several hours it may be used for agglutination tests (5). Our experience with agglutination tests using *Salmonella* and *Shigella* group sera was unsatisfactory in fluids containing urea. It was necessary, therefore, to disregard the excellent medium of Singer (6) for a rapid technic.

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A primary differentiating medium, called "booster" broth by Sanders (7), can be used for the serologic screening of Enterobacteriaceae. The small amount of growth present within 4 to 6 hours after incubation, however, does not allow one to carry out detailed agglutination studies. Since it is desirable to have duplicate cultures it appeared worthwhile to seek a second media which would provide the maximum additional information rather than to inoculate two tubes of "booster" media.

Within certain limits, semisolid mannitol will allow the differentiation of motile and non-motile organisms in a few hours, thus helping to distinguish *Shigellae* from many other Enterobacteriaceae. The absence of fermentation of mannitol will exclude *Proteus* with the exception of the rare *P. rettgeri*, and aid in establishing the groups of *Shigellae*. After a slightly longer incubation time using an iron indicator, even hydrogen sulfide formation can be observed in this medium.

After preliminary tests with different peptones and iron indicators, a modification of Felsenfeld's (8) semisolid mannitol was prepared. Additional sources of amino acids were employed in order to achieve faster growth and more rapid hydrogen sulfide production. The final formula of the medium is:

Mannitol .....	2 gm.
Meat extract .....	0.3 gm.
Sodium chloride .....	0.5 gm.
Tryptose .....	2 gm.
Agar .....	0.35 to 0.45 gm.
Ferric ammonium citrate ....	0.05 gm.
Sodium thiosulfate .....	0.05 gm.
L-cystine .....	0.02 gm.
Potassium diphosphate .....	0.03 gm.
Distilled water .....	100 ml.

Dissolve by gentle heating and adjust pH to 7.2 to 7.4, then add 0.6 ml. of an aqueous

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0.4% Brom thymol blue solution and 1 ml. of Andrade's indicator. Dispense in Wassermann tubes, 3 ml. each.

Sterilize by autoclaving at 10 lbs. pressure for 10 minutes. Keep in the refrigerator.

The amount of agar has to be varied according to the source of the batch of this ingredient. It is essential not to use media which has become dehydrated since motility and gas formation will be reduced.

This medium was tested with 123 Enterobacteriaceae and gave easily interpreted reactions within 4 to 6 hours. It was used then in combination with a lactose "booster" of the following composition:

Lactose .....	2 gm.
Tryptose .....	2 gm.
Sodium chloride .....	0.5 gm.
Meat extract .....	0.3 gm.
Distilled water .....	100 ml.

Dissolve by gentle heating and adjust pH to 7.2 to 7.4, then add 0.6 ml. of an aqueous 0.4% Brom thymol blue solution and 1 ml. of Andrade's indicator. Dispense in Wassermann tubes 1 ml. each.

Sterilize by autoclaving at 10 lbs. pressure for 10 minutes. Keep in the refrigerator.

These two media were tested in combination by employing artificial stools, i.e., a mixture of 24 hour tryptose broth cultures of one *Escherichia*, one *Aerobacter*, one *Proteus*, one *Paracolon* strain and one culture of a known *Salmonella* or *Shigella*. One hundred twenty-three *Salmonella* and *Shigella* strains were employed in this experiment.

The test procedure was:

The artificial stool was streaked to an S.S. and an E.M.B. agar plate. After 18 to 24 hours incubation at 37°C. each suspicious colony was picked to one tube of lactose booster and one tube of semisolid mannitol. These tubes were incubated for 5 hours and observed.

Table I, from which the results were evaluated, is

TABLE I

	Booster	Mannitol	Motility	H <sub>2</sub> S
<i>Salmonella typhi</i>	0	A	+	Slight or 0
Other <i>Salmonella</i>	0	AG	+	V
<i>Shigellae</i>	0	A or 0	0	0
<i>Proteus</i>	0	0	+	V
<i>Escherichiae</i>	+	AG	V	V
<i>Aerobacters</i>	+	AG	V	V
<i>Paracolons</i>	0	AG	V	V

0 = unchanged or non-motile.

± = changed or motile.

A = acid produced.

AG = acid and gas produced.

V = variable reaction.

based on observing the change of the indicator to yellow and red in both media. The appearance of gas bubbles along the line of inoculation in the semisolid mannitol indicates gas formation. Motility is read from the appearance of the line of inoculation; hydrogen sulfide formation by a brown to black discoloration in the semisolid medium. Typhoid strains often show limited motility (not extending to the periphery of the tube).

Agglutination tests, using the contents of the booster tube, were performed by the slide method. The sera were chosen according to the reactions observed in the semisolid mannitol, disregarding the hydrogen sulfide formation which was often slow. Only group sera were employed. One drop of the booster was mixed with one drop of the serum, and the reactions observed for 5 minutes. The growth in one tube of booster broth is enough for about 10 serologic tests.

The growth from the mannitol tube was used for transferring the culture to other media, including those used for the preparation of diagnostic antigens for detailed serologic studies.

One limiting factor of this method is the inability of inexperienced technicians to pick one colony to two media without contamination. If softer E.M.B. or MacConkey's plates (with less agar content) are employed, allowing the growth of larger colonies within a shorter time, sufficient material is then available within 16 to 18 hours to obviate this danger.

The method here described is not a substitute for the classic "long" technic of thorough bacteriologic examination, and in each case the classic technic should be utilized for confirmatory purposes. The proposed method simply allows a preliminary evaluation of cultures within 20 to 24 hours after the stool specimen reaches the laboratory.

#### SUMMARY

A method is described which permits the preliminary identification of *Salmonellae* and *Shigellae* within a short time. Each suspicious colony from the enteric plate is picked into two media; lactose broth and semisolid mannitol. If feasible, agglutination tests are conducted four to six hours later with the growth in the broth, using sera indicated by the reactions in the mannitol tube.

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## \*LAGAL®—A NEW AID FOR ATONIC CONSTIPATION

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LAGAL® HAS been introduced as the only bulk laxative available on the market that contains alginates as active ingredients. Alginates have been used in exceedingly low concentrations for many years as thickening and stabilizing agents in food products. Their use is particularly popular in ice cream where they will prevent, when present in concentration of about 0.1 per cent, the formation of ice crystals on storage. A study of the physical and physico-chemical properties of alginic acid and its salts has been carried out. Ludwig et al (1925) have found that alginic acid possesses ion exchange properties *in vitro* which compare favorably with those of a carboxylic type cation exchange resin. They found that the potassium and sodium alginate formed in the intestinal tract after ingestion of alginic acid have a markedly hydrophilic character and act as a bulk laxative. The physical properties of the bulking action of sodium and calcium alginate have been further studied by Berger et al (1953). The hydrophilic properties of alginates, as contained in Lagal, have been studied and compared with those of methylcellulose, carbomethylcellulose, psyllium seed and gum karaya. It has been found that the ability of alginates to retain water as well as the ability of alginates to absorb water is very much greater than that of any of the natural gums, methylcellulose or carbomethylcellulose. The sodium and calcium alginates also proved superior to the other bulk laxatives in not swelling in acid environment, thus being unlikely to cause fullness in the stomach as is frequently caused by methylcellulose or some of the natural gums that do swell in the acid environment of the stomach. The alginates have also been found to produce much more bulk for any given weight, thus enabling administration in smaller dosage. Lastly, the bulk produced by alginates proved friable so that the occurrence of impaction or obstruction as occasionally observed with other bulk laxative was unlikely to occur.

Fifty-seven patients with the chief complaint of constipation were selected from among clinic patients of the Gastro-intestinal clinic of the Jersey City Medical Center and from my own private office patients to provide a basis for evaluation of the efficacy of Lagal®. All patients were adults varying between the ages of nineteen to seventy-five. Constipation had existed for a minimum of ten years in all cases. In some instances constipation had existed for as much as thirty to forty years. An X-Ray examination of the colon by barium enema and sigmoidoscopy was done in every case. All cases were found to have an atonic form of constipation with one or more of the following findings: varying degrees of dilatation of the colon; pseudo-megacolon; redundant splenic or hepatic loops. Of the patients with severe degrees of constipation which had existed through a long life it was found necessary to give two teaspoonfuls of Lagal® twice daily; in milder

degrees of constipation two teaspoonfuls daily were sufficient. Eight glasses of water were given daily. Of the fifty-seven cases of atonic constipation nine patients reported no help from the use of the product, the remainder obtained excellent results so long as they used the product. In fourteen cases the patient was advised to use oil retention enemas and large doses of B complex for the first week or ten days along with Lagal®, after which they continued to use Lagal® without additional help. The great majority of patients reverted back to constipation as soon as they stopped the use of Lagal®. In eighteen cases methylcellulose products were used in place of Lagal®, and these appeared to yield the same effective results as Lagal®. In the remainder of the cases Lagal® appeared to give somewhat better results than the ordinary methylcellulose products used. An additional series of eighteen cases of spastic constipation as diagnosed by barium enema X-Rays and G-I series X-Rays was treated further to evaluate the usefulness of Lagal® in spastic constipation.

Lagal® appeared to give increased bulk in the spastic constipation cases, but the need for anti-spasmodics and sedatives was not alleviated by the use of Lagal®. In eight cases of spastic colon the condition was aggravated by the use of Lagal®. In the presence of hemorrhoids the use of the bulk laxative appears to aggravate the condition somewhat and some instances of thrombotic piles and increased bleeding was noted.

### COMMENT

Fifty-seven patients with atonic constipation and X-Ray evidence of varying degrees of dilatation of the colon, pseudo-megacolon and redundancy of the colon were treated with Lagal® alone or in addition to the use of large amounts of water, B complex and oil retention enemas. The use of Lagal® only was helpful in thirty-four cases or sixty per cent of the patients on whom it was tried. The use of Lagal® plus other help gave excellent results in ninety per cent of the cases of atonic constipation. In eighteen cases of spastic constipation ten patients appeared to be helped while eight cases were aggravated.

### CONCLUSION

Lagal® was found to be an excellent adjuvant in the treatment of atonic constipation, but it can only be used in about fifty per cent of spastic constipation patients because of the tendency toward aggravation of symptoms.

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\*Lagal® was supplied by the Wallace Laboratories of New Brunswick, New Jersey.

\*\*From the Gastro-intestinal Clinic of the Jersey City Medical Center, Jersey City, New Jersey.

## ABSTRACTS ON NUTRITION

MIRONE, L.: *Hemoglobin level and dietary intake of adults*. J. Clin. Nutr., 2, 1, Jan.-Feb. 1954, 38-42.

Because of the commonly held belief that hemoglobin levels were low in the Southern States, Dr. Mirone of the University of Georgia, Athens, Georgia, examined the hemoglobin in 535 adult residents of Georgia and, at the same time, took dietary histories on the same persons. Briefly, the hemoglobin levels were found normal. The average for 139 men was  $16.13 \pm 0.09$  grams, and for 396 women it was  $13.99 \pm 0.05$  grams. The dietary histories indicated that these individuals consumed diets well within the Recommended Allowances of the National Research Council. The fat intake was high, over 40 percent of the calories being derived from fat. Of the men, 23.8 percent were overweight and of the women only 9.1 percent. These findings may indicate that great benefit has been derived from the Nutrition Educational Programs carried out since World War II.

PUTON, A. AND PETCH, C. P.: *Association of diabetes mellitus with cerebral tumors*. Brit. Med. J., Apr. 10, 1954, 855-856.

A case is described in which diabetes mellitus of recent onset was associated at necropsy with a neoplasm in the region of the hypothalamus. The authors cannot avoid the feeling that the cerebral lesion was responsible for the onset of diabetes. There is some clinical and experimental evidence that the hypothalamus is concerned in the regulation of carbohydrate metabolism.

WOLF, S.: *A critical appraisal of the dietary management of peptic ulcer and ulcerative colitis*. J. Clin. Nutr., 2, 1, Jan.-Feb. 1954, 1-4.

Tension and anxiety can nullify the beneficial results of a high fat meal on gastric acidity and motility. One should not count very heavily on the inhibitory effects of diet in peptic ulcer when the stomach is under stimulation from stressful situations in the patient's daily life. There is a great need to study the true effects of certain so-called irritating foods, condiments and chemicals on the stomach. In a fistulous subject, the direct application of commonly accepted irritants produced fewer and lesser changes in the stomach than on the skin. Similarly, the colon in ulcerative colitis responds more violently to certain situational stimuli than to foods and fecal contents.

SHUMAN, C. R. AND WOHL, M. G.: *Nutritional aspects of heart failure*. J. Clin. Nutr., 2, 1, Jan.-Feb. 1954, 5-10.

As cardiac decompensation increases, nutrition becomes increasingly affected—changes in the electrolyte and water balances, hypoproteinemia and subclinical thiamine deficiency. Anorexia, impaired absorption and utilization of nutrients are responsible. While mercurial diuretics are life-prolonging, they greatly increase thiamine excretion. A diet with adequate protein, restricted salt and the use of vitamins is recommended.

JULY, 1954

PROF. GRANDE: *The physiological role of zinc and its relations with carbohydrate metabolism*. Rev. Espan. Enf. Del Ap. Dig. Nutr., Vol. XII, 5, 433, Sept.-Oct. 1953.

The author adduces the lack of positive arguments with reference to the part played by zinc in the metabolism of the carbohydrates. Many of the facts used in medical literature up till now have not been correctly interpreted and others are incompatible with present day knowledge. There is no proof at all that zinc forms part of the insulin molecule as this incretion is formed by the pancreas. On the other hand, zinc is not necessary in order that insulin may perform its physiological role. The abundance of zinc in the pancreas seems to be in relation to the exocrine activity of this gland, there being no existing proofs of the concentration of this metal in the islands of Langerhans, but, on the other hand, there are proofs of its presence in the acinus cells.

In the animals experimented on, the deficiency of zinc does not cause specific disorders in the metabolism of the carbohydrates nor, on the other hand, has any change in zinc metabolism been proved in human diabetes.

The combination of alloxan and zinc does not explain the diabetogenic action of this substance, as one deduces from the following facts: (1) Alloxan does not inhibit the activity of carbonic-anhydrase, the only zinc compound with known physiological action; (2) Among the many agents capable of combining with zinc, only two—oxine and ditizone, have shown diabetogenic activity, according to some authors; (3) the diabetogenic effect of oxine and ditizone appears to be limited to the rabbit and there is no evidence of this substance in other animal species, particularly sensitive to the diabetogenic action of alloxan.

While accepting Wolff's hypothesis with regard to the part played by zinc in the diabetogenic action of alloxan, this does not presuppose in any way that zinc plays a physiological part in the process of the formation of insulin. More so, if one takes into account that neither have we definite proof that alloxan plays a physiological role in the regulation of the production of the hormone of insulin.

GROSSMAN, C. M. AND MALBIN, B.: *Mushroom poisoning: a review of the literature and report of two cases caused by a previously undescribed species*. Ann. Int. Med., 40, 2, Feb. 1954, 249-259.

Mushroom poisoning, though not common in Great Britain and the United States, is prevalent throughout the world, especially in Europe. The most common causes of poisoning are the species, *Amanita phalloides* and *Amanita muscaria*. *A. phalloides* produces severe damage to the liver, kidneys and central nervous system and is responsible for most of the fatal cases. Two cases of mushroom poisoning by a previously undescribed specimen of the genus *Galerina* (*G. Venenata* Smith) are reported. One of the patients suffered se-

vere damage to the gastro-intestinal, renal, cardiovascular, hepatic and central nervous systems, including a complete adynamic ileus, followed by recovery. In the muscarine type of poisoning, atropine is considered specific. In other forms, general supportive measures, and the use of glucose and electrolytes is indicated.

MUTSUKA, S.: *On the fluctuation of amino-nitrogen content of peripheral blood in patients after total gastrectomy.* Kyushu Memoirs of Med. Sci., 4, 1, Sept. 1953, 51-59.

The authors found that the ingestion of beef in rather sizable amounts, in persons who had had total gastrectomy done, produced a condition of temporary hyperaminoacidemia. This was caused by the sudden introduction of large amounts of meat into the intestine. Owing to the loss of the stomach as a reservoir, there was not the usual and normal, gradual entrance of protein food into the intestine.

HUDSON, F. P., IRELAND, J. T., OCKENDEN, B. G. AND WHITE-JONES, R. H.: *Diagnosis and treatment of galactosaemia.* Brit. Med. J., Jan. 30, 1954, 242-245.

Galactose, formed during the metabolism of lactose, is normally converted into glycogen in the liver. In galactosaemia ("galactose diabetes") this process is defective, resulting in a high concentration of galactose in the blood and its excretion in the urine. Galactose,

in such concentrations, probably is toxic and responsible for the main lesions of the disease—hepatic cirrhosis, cataracts and albuminuria. The earliest signs appear soon after birth, the child failing to gain weight and being reluctant to feed. Jaundice is common but varies in intensity. Basically, the treatment consists in removing lactose from the diet. If begun early, all manifestations of the disease may disappear. Mental impairment has persisted in some of the published cases but possibly early treatment might prevent this. The galactose-tolerance test is likely to remain permanently abnormal.

PERKIN, F. S. AND DERBYSHIRE, A. J.: *Carbohydrate metabolism in the convulsive state.* Harper Hosp. Bull., II, 6, Nov.-Dec. 1953, 248-257.

A group of 76 proven convulsives (epileptics) not sufficiently severe or deteriorated to require institutional care was studied over periods varying from one to seven years. The study was initiated by the observation of epilepsy beginning during periods of hypoglycemia resulting in brain damage. Long-term glucose tolerance tests gave results suggesting a rather frequent abnormality of carbohydrate utilization. Studies of serum inorganic phosphorus co-incident with glucose tolerance tests tended to confirm this impression. The problem of labile diabetes may be related to this conception. The hitherto unreported high incidence of diabetes in the family history of individuals manifesting epilepsy is, if confirmed, of utmost significance.

## EDITORIALS

### ACUTE APPENDICITIS

In spite of all we know about the treachery of acute appendicitis, there are 2,600 persons dying annually of the disease in the United States alone. It is fallacious to think that the diagnosis and treatment of acute appendicitis is an easy matter. Because of the volumes which have been written on the subject, the average physician usually feels that there is nothing further to be said. But there is always this, *that each case is, in some respect, unique.* There is practically no symptom which may not be absent in a given case. I remember one case in which there was normal temperature, normal white blood count, no vomiting, no pain and only a very slight degree of resistance of the right rectus muscle, yet on opening the abdomen the appendix had ruptured and the peritoneal cavity was full of colon bacillus pus.

"Any bellyache may be appendicitis." "Suspect the appendix until it is proved innocent." These are only two of the well-known aphorisms which should never be forgotten. Because an appendiceal abscess has formed is actually poor reason to be complacent. To rely upon antibiotics without surgery in the treatment of a suspected acute appendicitis is not an admirable form of bravery.

Boyce (1) has recently summarized the situation in excellent fashion and his article should be read particularly by physicians.

1. Boyce, F. F.: The role of atypical disease in the continuing mortality of acute appendicitis. *Ann. Int. Med.*, 40, 4, April 1954, 689-693.

### ANEMIA IN THE SOUTHERN STATES

From time to time, we have made editorial reference to the alleged anemia which was considered to be prevalent throughout the South. Many articles have appeared in medical journals during the past 10 years to indicate that many, if not the majority of persons living in the South, were somewhat anemic as compared with standards in the Northern States. It has been stated that, even among "good livers" in the South—people who ate the best of food and sufficient of it—there was a tendency to show rather low hemoglobin levels and red blood cell counts. Talking with physicians in the South has always confirmed this fact. These doctors usually expressed their opinion to the effect that Southern-grown produce and animals actually were deficient in blood-building elements, because of some lack in the soil.

However, the recent work of Leonora Mirone, Ph.D. (1) of the University of Georgia, Athens, Georgia, if confirmed, would appear to indicate that the Nutrition Educational Programs carried out since World War II had altered the situation. In fact, in a rather extensive survey of hemoglobin levels, and of dietary intakes in Georgian people, she found the hemoglobin levels at a high normal and the diets generally adequate in all respects.

If Dr. Mirone's work is confirmed, we must then conclude that eating habits rather than soil deficiency caused the general anemia which previously had been well documented.

1. Mirone, L.: Hemoglobin level and dietary intake of adults. *J. Clin. Nut.*, 2, 1, Jan.-Feb. 1954, 38-42.



## BOOK REVIEWS

PHYSIOLOGY AND PATHOLOGY OF THE BILIRUBIN METABOLISM AS FUNDAMENTAL FOR THE RESEARCH OF ICTERUS. (PHYSIOLOGIE UND PATHOLOGIE DES BILIRUBINSTOFFWECHSELS ALS GRUNDLAGEN DER IKTERUSFORSCHUNG). Tr. Baumgaertel. 271 pg., 2 illustrations. DM 27.00 Thieme Verlag, Stuttgart 1950.

This book contains an historical and critical analysis of the physiology and pathology of the bilirubin metabolism. All important and relevant facts are mentioned, and the results of research in chemical, biological and clinical pathological fields relating to the problem, are thoroughly discussed. Baumgaertel is well known to all who are interested in this field, for his publications are of fundamental importance. Very important is his critical analysis of icterus as a "disturbance of the bilirubin metabolism." The book is written in German and contains innumerable references. It can be recommended to all who are interested in this field.

Franz J. Lust.

WINE AS FOOD AND MEDICINE. Salvatore P. Lucia, M.D., etc. The Blakiston Company, Inc., New York, 1954. \$3.00.

It is possibly unfortunate that in this country wine is seldom thought of either as a medicine or a food.

There are very few American physicians who prescribe wine for medical or nutritional purposes. In France, on the contrary, a physician's advice and prescription usually specifies wine, what kind of wine and how much. The present volume is very interesting to anyone who loves wine. It shows that when used in moderation, various wines exert a favorable effect on the health of the patients, usually as a metabolic stimulant. The chemistry of wine is reviewed. The unfavorable aspects of over-indulgence are not omitted. If moderate wine-drinking could replace the use of spirits, as in cocktails and "highballs," it would be advantageous.

CONFRONTATIONS - RADIO-ANATOMO-CLINIQUES. M. Chiray, R. A. Guttmann, and J. Seneque. G. Doin & Co., Masson & Co., Paris, 1954. 1800 francs.

The fifth in a series, this volume presents cases of gastrointestinal disease in such a way that the history, physical examination, x-ray films, specimens or slides are all conveniently grouped together, with comments by experienced gastroenterologists. One cannot praise too highly the general structure of the book and particularly the excellent x-ray reproductions. Even though it is written in French, it is not difficult for the English reader to gain the correct sense in each presentation.

## GENERAL ABSTRACTS OF CURRENT LITERATURE

PABLOS, ABRIL, J.: *Chirurgical treatment of acute cholecystitis*. Rev. Espan. Enf. Del Ap. Dig. Nutr., Vol. XII, No. 2, 144-172, March-April 1953.

The writers study the surgical treatment of acute cholecystitis. They are in favor of early operation in the first 48 hours, provided that the general condition and hepatic state of the patients are good and they are not of advanced age. This procedure is the best prophylactic means of preventing serious complications which may result from that morbid process. After the first 48 hours, surgical treatment should be restricted to complicated and persistent conditions.

They review their material (42 cases) operated upon in the last six years. In these cases surgical treatment was employed in a systematic way. Only those cases showing slight involvement or those in which there were operative counter-indications were not operated upon. Immediate death rate was 7 percent. Cholecystectomy was performed in 80 percent of cases, and palliative operations in the remaining 20 percent. The operative methods and complications are reviewed. Finally, a brief summary of the casuistics is given with roentgenographs and photographs of some cases.

JULY, 1954

BERGARACHE, J.: *Posthydatid bilio-bronchial fistula*. Rev. Espan. Enf. Del Ap. Dig. Nutr., XII, 3, 260-276, May-June 1953.

The writer studies the pathogenesis and clinical development of a case of bilio-bronchial fistula which resulted from a long-standing hydatid cyst in a "marsupialised" liver. Surgical operation revealed that it was not a direct cysto-bronchial but a bilio-bronchial fistula produced by angiocholitis, with a focus of primary infection in the residual pericystic cavity, situated on the lower aspect of the liver, far from the diaphragm.

SITGES CREUS, A.: *Treatment and physiopathology of cardiospasm*. Rev. Espan. Enf. Del Ap. Dig. Nutr., XII, 3, 294-317, May-June 1953.

The writer studies the physiology, etiopathogenesis and treatment of cardiospasm. Treatment should be based on forced instrumental dilatation of the cardia. Surgical treatment should be restricted to advanced cases of cardiac fibrosis or to those cases in which the instrument cannot be introduced owing to incurvations in an enlarged esophagus. These circumstances, however, are extremely rare. Psychotherapy should be tried only on early cases in which anamnesis reveals that psychic shock plays a leading role.



VIAR BAYO, J. AND OBREGON, J. L.: *Serum Hepatitis*. Rev. Espan. Enf. Del Ap. Dig. Nutr., XII, 3, 247-260, May-June 1953.

The writers report 7 cases of hepatitis which occurred within 50 to 105 days after blood transfusions. In two cases the course was short and death ensued (the death-rate being, therefore, 28 percent). In the light of such accidents they strongly recommend that the clinical history of blood donors be always studied and those who have suffered from jaundice rejected. An analysis should be carried out for the presence of urobilin or bilirubin in the urine of those who do not mention this pathological antecedent.

As regards treatment of hepatitis, in addition to an adequate diet containing carbohydrates and proteins, vitamins B, C and K, and injections of glucose and levulose, and of amino acids in cases of anorexia or mental disturbances, should be given. With regard to antibiotics, terramycin may be prescribed. The use of cortisone, ACTH and total extracts from adrenal cortex likewise proves effective.

BADOSA GASPARD AND GALLART-ESQUERDO, A.: *Clinical value of the secretin test in several pancreopathies*. Rev. Espan. Enf. Del Ap. Dig. Nutr., XII, 3, 231-237, May-June 1953.

From their experience, based on over 100 pancreatic function tests with secretin, the writers draw the following conclusions: 1. In normal subjects, the pancreatic juice obtained by means of the duodenal tube five minutes after intravenous injection of 40 to 80 units of pure crystallised secretin contains bile and duodenal juice in varying proportion. The lipase content of this juice are far superior to those seen before the stimulating injection. 2. The decrease in the lipase contents of this juice first extracted, five minutes after the intravenous injection of secretin, should be regarded as pathological. 3. Carcinoma of the head of pancreas gives origin to a remarkable decrease, or to a complete absence of the pancreatic ferments usually present in the duodenal juice. If, in addition, there is obstruction of the common bile duct, the duodenal juice extracted appears white and appropriate tests will reveal absence of bile. In cases of carcinoma of the body and tail of pancreas the secretin test gives normal results. For this reason the writers hold the view that the absence of pancreatic ferments from the duodenal juice, or the decrease in the amount of them indicate terminal obstruction of Santorini's duct and Wirsung's canal rather than invasion of the gland by neoplasm. 4. The lipase secretion graph obtained in cases of chronic icteric pancreatitis with involvement of the head of the gland is extremely similar to that obtained in cases of neoplasm. 5. In a case of necrotic pseudocyst of the pancreas the total volume of pancreatic juice and the coefficient of mean fat-splitting activity were found to be remarkably increased. In a case of cysto-adenoma of the head of pancreas completely inverse results were obtained.

ORTIZ VAZQUEZ, J. AND ALFONSO RIBERA, E.: *Fever and gastric cancer*. Rev. Espan. Enf. Del Ap. Dig. Nutr., XII, 5, 493-502, Sept.-Oct. 1953.

The writers report a case of carcinoma of the stomach attended with two exceptional features: its oc-

currence in early age (18 years) and its clinical picture of merely febrile nature for several months in its initial development. The infrequency of both circumstances justifies late diagnosis.

DAVIES, R. M., MOORE, F. T. AND WYNN-WILLIAMS, D.: *Treatment of acute pancreatitis with hexamethonium bromide*. Brit. Med. J., Dec. 5, 1953.

Two cases of acute pancreatitis are described in which recovery occurred following the use of oral hexamethonium bromide (e.g. 250 mg. twice daily, via indwelling stomach tube). The authors believe that acute pancreatitis is due to a "vascular catastrophe," namely, thrombosis or embolism of a main pancreatic vessel. The drug used acts to produce a splanchnic block. Further investigation is required.

MILLS, G. Y. AND KAGAN, B. M.: *Effect of oral polymyxin B on pseudomonas aeruginosa in the gastro-intestinal tract*. Ann. Int. Med., 40, 1, Jan. 1954, 26-32.

Oral polymyxin B (Aerosporin, B. W. and Co.) is very effective in eliminating *P. aeruginosa* (*B. Pyocyaneus*) when it is present in the gastrointestinal tract either in carriers or in active infections. Such infections in children frequently become generalized and prove fatal. 150 mg. of the drug were given orally every 8 hours for 7 days. Mild cramps and diarrhea may occur at first, as side effects, but later disappear.

ROBERT, W. E.: *Carbonated soft drinks in roentgen diagnosis of foreign bodies in the stomach*. Am. J. Roent., Rad. Ther. and Nuc. Med., 71, 2, Feb. 1954, 239-242.

An important fact to be remembered in using carbonated soft drinks, as a contrast medium, for localizing foreign bodies in the abdominal visceral cavity is to use them cold, and in small quantities. Large amounts frequently give false impressions. This medium is useful in demonstrating, by contrast, foreign bodies of slight radio-opacity. Soft drinks may be conveniently used to outline the stomach where position is the only consideration, as in *situs inversum viscerum*. Carbonated drinks, however, may be of little value immediately after a meal.

BURROWS, R. B.: *Intestinal parasitic infections in military food handlers*. U. S. Armed Forces Med. J., V, I. Jan. 1954, 77-82.

1500 military food handlers were examined for intestinal parasites and 10 percent were found to harbor pathogenic species. The incidence found in the Air Force was higher than that in the Army or Marine Corps personnel. Army enlisted men in the higher grades, who probably had more overseas service, showed a higher incidence than those in the lower grades, who probably did not have overseas service. Military personnel have a higher incidence for nearly all helminth infections than civilians in the U.S.A. The general population has only an estimated 4.1 percent incidence.

GOODALL, J. F.: *The winter vomiting disease*. Brit. Med. J., Jan. 23, 1954, 197-8.

Goodall, a general practitioner, describes small

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epidemics of the so-called "winter vomiting disease" (or hyperemesis hiemalis). Usually the patient, who has been perfectly well, wakes in the morning with severe vomiting, often associated with collapse. In one or two days, recovery is complete. Serological tests in nine cases showed no connection with influenza. It must be differentiated from food poisoning, dysentery, hepatitis, appendicitis and upper respiratory infections in children. Goodall does not think there is any such entity as "stomach flu." The etiology of the condition is unknown.

MOORE, T. C.: *Acute spontaneous volvulus of the right colon with gangrene.* J. Indiana State Med. A. March 1954, 47, 3, 237-240.

A case is presented in which the acute onset, lower right quadrant guarding, with severe abdominal pain, suggested appendicitis. Operation revealed volvulus of the right colon with gangrene. The terminal ileum and right colon were resected and the ileum anastomosed to the transverse colon. The patient made a good recovery. Volvulus of the right colon is one of the rarest conditions producing symptoms of acute surgical abdomen.

GOLDENBERG, M. M.: *Congenital absence of the gallbladder.* Illinois Med. J., 105, 3, March 1954, 123.

Goldenberg says there are only 75 cases of congenital absence of the gallbladder in the literature. He reports a case. The symptoms suggested gallbladder disease, although repeated attempts to visualize the organ with telepaque were unsuccessful. At operation, no gallbladder could be found. The common duct was larger than normal. Draining the common duct for a time with a T-tube brought about recovery from her symptoms.

BAUMEISTER, C. F.: *A new treatment for pruritus ani.* Journal Lancet. Nov. 1954, 89.

Baumeister has found the local application of a cortisone ointment extremely effective in controlling the symptoms of pruritus ani. In some cases the treatment has to be continued indefinitely. The hard, glazed skin which sometimes forms in the peri-anal region has to be softened before application of cortisone ointment.

JACOBSON, G. AND HEITMAN, K. A.: *Cholangiography with a viscous, water-soluble contrast medium (diodrast in methylcellulose).* Radiology. Feb. 1954, 62, 2, 241-244.

35 percent Diodrast in 1 percent methylcellulose as a contrast medium for cholangiography is shown to have several advantages. It forms a continuous column, being miscible with bile, and there is none of the disturbing globule formation seen so frequently with oily media. The density is such as to permit adequate fluoroscopic visualization and good films, yet not so great that small radiolucent stones contained in the large dilated common duct are obscured. No reactions attributable to the Diodrast or methylcellulose have been observed.

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BERMAN, E. J. AND ERXLEBEN, W. O.: *Pancreatitis.* J. Indiana State Med. Assn., Mar. 1954, 47, 3, 243-248.

117 cases of pancreatitis were studied in 3 hospitals in Indianapolis. The most interesting fact disclosed relates to the prognosis in acute hemorrhagic pancreatitis. It was found that in this disease twice as many deaths occurred in cases treated medically as in those treated surgically. This finding is contrary to recent attitudes developed toward the management of acute pancreatitis.

SHAPIRO, R.: *Cholecystography.* Radiology, Feb. 1954, 62, 2, 245-247.

Shapiro enumerates the well-known extra-cholecystic factors which may operate to cause non-visualization of the gallbladder. He emphasizes one factor, usually not considered. This is lactation. Olsson has shown that non-visualization may occur in lactating mothers due to excretion of tetraiodophenolphthalein in the milk.

CAMERON, G. R.: *The liver as a site and source of cancer.* Brit. Med. J., Feb. 13, 1954, 347-352.

In an eloquent lecture, devoted largely to what we do not know about metastatic cancer, Cameron makes a plea for a keener understanding of cancer metastases. He thinks we should try to find ways of circumventing the growing tumor by inhibiting or suppressing its powers of growth, by turning it aside into more innocuous channels, perhaps by throwing obstacles in its pathways of spread or even sacrificing healthy tissues in order to hold up the neoplastic invader by means of a "burnt earth" policy. He shows that the liver is the most vulnerable organ for cancer metastasis.

WITTER, J. A. AND FIRST, M.: *Ligation of the hepatic and splenic arteries for advanced periportal cirrhosis.* Alex. Blain Hosp. Bull., 12, 1, Nov. 1953.

The authors describe a simple manometer for determining portal pressures. Portal hypertension usually is due to the intrahepatic blockage which accompanies Laennec's cirrhosis. It can be demonstrated that the portal pressure is markedly reduced in some of these cases by ligation of the splenic and hepatic arteries. Such ligations are technically easier to accomplish and are less time-consuming than venous shunts. Two cases are presented.

CROMBIE, T. G.: *Diagnostic difficulties in conservative treatment of perforated ulcers.* Brit. Med. J., Feb. 13, 1954, 374-377.

Crombie takes the attitude that when perforation of a gastric or duodenal ulcer is made, operation should be done, provided the patient's condition warrants operation. He spends some time in describing conditions which may imitate perforation of an ulcer—tabetic crisis, diaphragmatic pleurisy, coronary infarction and acute cholecystitis. He emphasizes that "peritoneal irritation" may arise from perforations elsewhere. He is not in favor of non-operative treatment of perforated ulcer unless the patient's general condition is bad.

HOLMES, T. W.: *An evaluation of celiac ganglionectomy in the prevention of experimental peptic ulcer*. Alex. Blain Hosp. Bull., 12, 1, Nov. 1953.

Little attention has been paid to the sympathetic nervous system in the management or prevention of peptic ulceration. Sympathetic denervation is helpful in pancreatic dysfunctions, but has not been tried as a possible instrument in the control of duodenal or gastric ulcer. In experiments on albino rats, gastric ulceration produced by the pylorus ligation method was significantly reduced by simultaneous or preliminary celiac ganglionectomy, though less effective than simultaneous vagotomy. Further investigations are being done to classify the anti-ulcerogenic effect of celiac ganglionectomy.

SAN JULIAN, J. S.: *Observations on pancreatic fistula*. Rev. Espan. Enf. Del Ap. Dig. Nutr., Vol. XII, 3, 237-247, May-June 1953.

The writer describes a series of experimental observations carried out in a case of pancreatic fistula. He concludes that the volume of pancreatic secretion, when a mixed diet is given, reaches its peak after the midday meal and is lowest after breakfast. The greatest volume corresponds to meals based on carbohydrates. Injection of anticholinergic drugs causes the volume of secretion to diminish remarkably; the ferment contents are likewise decreased. In this connection Banthine is the most powerful drug. The amount of amylase present in the blood and urine is decreased, together with the volume of secretion, after administration of Banthine or atropine to the patient. Adrenalin gives rise to a decrease in the volume and pancreatic secretion of amylase and to hyperamylæmia.

PABLOS ABRIL, J.: *Absence of gall bladder*. Rev. Espan. Enf. Del Ap. Dig. Nutr., Vol. XII, No. 6, 596-600, Nov.-Dec. 1953.

A case is reported of absence of the gall-bladder, a rare anatomic abnormality in the human, observed in the course of a surgical operation for a suspected "calculous cholecystitis."

PALMER, EDDY, D.: *Diagnostic errors in severe gastro-intestinal hemorrhage*. U.S. Armed Forces M. J., V, 3, March 1954, 350-356.

Because every instance of hematemesis must be considered of urgent importance, and because medical and surgical techniques are available for direct attack on many of the lesions which may be responsible for massive upper gastrointestinal hemorrhage, it is particularly important that a precise diagnosis be made without delay. A vigorous diagnostic approach, consisting of esophagoscopic, gastroscopic and x-ray studies during the first few hours of hospitalization, has proved both safe and feasible. The present review

of 212 patients with hematemesis who were treated on the basis of history and physical findings alone revealed an important amount of diagnostic error, with inadequate therapy as a consequence. The highest single cause of bleeding was esophageal varices (68) with duodenal ulcer a distant second (32).

SAITO, H., ITO, C. AND KOIZUMI, M.: *Clinical investigations on epidemic hepatitis. Report II. Studies of the dye-test (hepatosulphalein test) for excretory function of the liver, and on the cadmium reaction*. Nagoya M. J., I, 3, July 1953, 187-192.

The bromsulphalein test was done on 11 cases of epidemic hepatitis, several times during the course of the disease. The grade of retention of the dye at 5 minutes showed maximum of 60 percent and minimum of 10 percent. It decreased gradually during convalescence. In 10 of the cases there were no remarkable changes in specific gravity and protein content of the blood serum. In 10 cases the cadmium sulfate reaction was positive but the cadmium chloride reaction was practically within normal limits. There was some relation between the cadmium sulfate reaction and the gamma-globulin in the blood serum, but the cadmium chloride reaction showed no such relationship.

PROF. BASSI: *The gastrograph and the combined study of gastric secretions and duodenal jejunal and gastric motility*. Rev. Espan. Enf. Del Ap. Dig. Nutr., Vol. XII, 4, 327-341, July-Aug. 1953.

The author resumes the clinical investigations which he has been carrying out during the past twenty years, with regard to the gastrograph and its application in the study of human gastric diseases. He also studies by means of this technique, the moving activity of the stomach under the action of different pharmacodynamic substances. On occasions he associates the pneumogastogram and the electrogastogram in his work, with the help of impolarizable electrodes placed in the interior of the stomach and of an osilographic mirror. He studies by means of various techniques the parallelism of gastric and duodenal secretions and of the motility of the stomach.

MARSELL, PINOS AND GALERA, GARCIA: *Histotherapy in the gastroduodenal ulcer*. Rev. Espan. Enf. Del Ap. Dig. Nutr., Vol. XII, 4, 352-366, July-Aug. 1953.

The authors test Filatov's therapeutics on a series of patients afflicted with gastric and duodenal ulcers. The results are not brilliant, especially from the radiological point of view, as the persistence of the ulcerous recess is a frequent occurrence, even though it is true that they were dealing with patients who had already withstood other therapeutic techniques. The most favorable action of histotherapy is revealed on the symptom of pain, increase in weight and psychism.



## CABBAGE AND TURNIPS

The following is an abstract of a paper given recently by Dr. Isidor Greenwald at a meeting of the Federation of American Societies for Experimental Biology in Atlantic City. Dr. Greenwald is professor emeritus of chemistry at New York University-Bellevue Medical Center's College of Medicine.

*Cabbage and Turnips as a Cause of Endemic, or of Epidemic, Goiter*

In recent years, there have been several reports in which a large consumption of cabbage or turnips has been held responsible for outbreaks of goiter in man and in sheep. Dr. Greenwald showed that the amounts eaten of such foods were not remarkably large.

In France, about 100 years ago, many families are known to have eaten much greater quantities, yet were perfectly healthy. Statistics for London indicate a similar large consumption of cabbage and of turnips. The figures from Germany, from 1909 to 1930, show an average consumption so large that there must have been many who ate quantities greater than those that have been supposed to have caused goiter. (In 1927-8, one German family spent 35 times as much for cabbage as did a similar family in the same city. Other families, in the same and other cities, showed similar, though smaller, differences.)

Turnips have been used in the winter-feeding of sheep in New Zealand for many years and for a much longer time in England. However, the only known instance of goiter was on one farm in New Zealand. There was no indication that the amounts of turnips used were at all unusual.

## SURVEYS OF FOOD AND NUTRITION RESEARCH IN THE U. S.

LeRoy Voris and Helen L. Jeffrey  
Food and Nutrition Board, National Research Council, Washington, D. C.

Comprehensive listings of active projects in food and nutrition research, the laboratories, supporting organizations, and professional research personnel engaged in the research have been published as the results of surveys conducted by the

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Food and Nutrition Board for 1947, 1948-49, and 1952-53. These publications included 4000 to 4800 projects, between 600 and 660 organizations conducting or supporting research and the names of about 5000 professional research workers. The research was classified by subject categories relating to physiology and biochemistry, food chemistry, food technology, microbiology, food acceptance, and nutrition education.

Of the research projects recorded, approximately 40 per cent pertained to nutrient metabolism and requirements (physiology), 30 per cent to food chemistry and composition, 20 per cent to food technology, and 10 per cent to microbiology, food acceptance, and nutrition education.

Between 1947 and 1953 there has been a possibly significant increase in number of projects devoted to food technology and a decrease in the number devoted to food chemistry and composition.

Of the organizations listed, approximately 50 per cent were industrial, 40 per cent academic, and 10 per cent governmental.

The objective of the surveys has been to provide a published guide for research workers to use in finding promptly what research was being done in a field of interest, where it was being done and how financed, and who was doing it.

The third survey was supported by contract with the U. S. Department of Agriculture, and the published volume will be available through the Government Printing Office.

## PARKE, DAVIS &amp; CO. INTRODUCES NEW TABLET FROM ANTICOAGULANT

Parke, Davis & Company has introduced a new tablet form anticoagulant for treatment of such conditions as thrombo-embolic disease, both real and threatened.

The new drug—called Indon—is effective orally and gives a more rapid onset of therapy for a shorter duration of action than "Dicumarol."

Dosage schedule for Indon, to be used only on physician's prescription, is six to eight tablets initially, followed in the next 24 hours by six tablets in divided doses.

Dosage should be governed by prothrombin determination (quick method). For maintenance, one to four tablets daily in two divided doses is usually sufficient.

"Since use of heparin and of 'Dicumarol' has become widespread in treatment of patients with various thrombo-embolic manifestations, certain deficiencies in actions of these two substances have stimulated continued search for drugs of similar activity which will retain advantages but avoid some disadvantages of these products," Parke-Davis stated.

"Indon is such a compound with its action lying somewhere between those of heparin and 'Dicumarol'."

A Canadian medical journal report said that phenylindandione was used in a controlled study on 20 patients and proved to be a safe drug which acts in about one-half the time as "Dicumarol" and is rapidly catabolized.

The Northwestern University Medical School reported in its Quarterly Bulletin that phenylindandione therapy brought the prothrombin level desired in 22 patients within 24 hours, and, in all patients in the series, the lowered level was reached within 48 hours.

Each Indon tablet is grooved, contains 50 mg. of phenylindandione (2-phenyl-1,3-indandione) and comes in bottles of 100.

## "CONQUERORS OF YELLOW FEVER"

Presented to Army Medical Graduate School by Wyeth Laboratories

"Conquerors of Yellow Fever," a painting of one of the great moments in medical history from among the Wyeth Laboratories collection, "Pioneers of American Medicine," was presented to the Army Medical Service Graduate School in Washington recently.

Dr. George E. Farrar, Jr., medical director of Wyeth Laboratories, made the presentation at a ceremony in the Walter Reed Army Medical School. Colonel William S. Stone, USA (MC), commandant of the school, accepted the painting for the Center. Dr. Farrar expressed the hope that the painting "may help continue to build the pioneer spirit among the Army Medical Corps which the event in the painting symbolizes."



Dr. Farrar went on to say that Wyeth Laboratories recognized many years ago that the citizens of our country knew little if anything concerning contributions to the health and welfare of our nation made by their own physicians.

"In order to pay proper and fitting tribute to those doctors who labored in anonymity, but whose work was of singular importance, Wyeth proposed to execute a series of paintings which would recapture great moments in U. S. medical history," he said.

The series was painted by the distinguished illustrator and muralist, Dean Cornwell, N.A. A panel of physicians selected the important moments in American medical history for re-creation. Months of investigation and research went into preliminary work on each painting.

With Major Walter Reed and Dr. Carlos Finlay looking on, the painting shows Dr. Lazear, who died a month later as a result of self-experimentation, inoculating Dr. Carroll with an infected mosquito. The event occurred on the grounds of Columbia Barracks Post Hospital of the United States Army in Cuba August 6, 1900.

This experiment indicated that the mosquito was the carrier of yellow fever.

#### PARKE, DAVIS & COMPANY ESTABLISHES NEW BRANCH IN SOUTH AFRICA

Establishment of a South Africa branch of Parke, Davis & Company was announced recently by W. R. Jeeves, vice-president and director of overseas operations, following a 26,000-mile business trip abroad with Harry J. Loynd, president.

The sales office of the new branch—the firm's 19th outside the United States and Canada—is located in Johannesburg (Leisk House, Bree and Rissik Streets). Manufacturing facilities have been set up in Port Elizabeth, on the tip of South Africa, Southwest of Johannesburg.

Jeeves said, "This new member of the overseas branches of Parke, Davis & Company will develop our existing interests in the Union of South Africa and the Rhodesias, serving those areas with products manufactured by us in Port Elizabeth. Later, its activities will be extended to other countries, terri-

tories and colonies in the continent."

E. H. Lambert, who has served more than 28 years with Parke-Davis in Great Britain, is general manager of the South Africa branch. He joined the London branch in October, 1925, as a sales representative and was promoted to assistant home sales manager in 1945, home sales manager in 1946, general sales manager in charge of both home and overseas sales in 1947, and joint assistant general manager in 1951.

Loynd and Jeeves inspected the South Africa facilities during their three-week flight from Detroit to London, Rome, Cairo, South Africa, Belgian Congo, Dakar, Lisbon and back to Detroit. While in London, they visited the firm's new research and administrative building, now occupied. In South Africa, they talked to medical, pharmaceutical and business leaders at Pretoria, Capetown and Durban, as well as those in Johannesburg and Port Elizabeth. They also visited Lourenco Marques in Portuguese East Africa.

The firm's Overseas Division maintains a sales and medical service staff of over 400 people with 50 different nationalities. Besides the 19 overseas branches, there are more than 70 major distributors elsewhere abroad, with representatives in virtually all other countries of the free world.

Loynd said, "The volume of business done abroad provides a stabilizing influence, and our demonstrated ability to operate profitably in other parts of the world offers opportunity for substantial additional expansion and growth."

#### INTERNATIONAL ACADEMY OF PROCTOLOGY 1954-1955 AWARD CONTEST

The International Academy of Proctology announces its Annual Cash Prize and Certificate of Merit Award Contest for 1954-1955. The best unpublished contribution on Proctology or allied subjects will be awarded \$100.00 and a Certificate of Merit. Certificates will be awarded also to physicians whose entries are deemed of unusual merit. This competition is open to all physicians in all countries, whether or not affiliated with the International Academy of Proctology. The winning contributions will be selected

by a board of impartial judges, and all decisions are final.

The formal award of the First Prize, and a presentation of other Certificates, will be made at the annual Convention Dinner Dance of the International Academy of Proctology, in March 1955. The International Academy of Proctology reserves the exclusive right to publish all contributions in its official publication, "The American Journal of Proctology." All entries are limited to 5,000 words, must be typewritten in English, and submitted in five copies. All entries must be received no later than the first day of February, 1955. Entries should be addressed to the International Academy of Proctology, 43-55 Kissena Boulevard, Flushing, New York.

#### BIG POTENTIAL FOR 'POP' CANS SEEN BY CANCO

A potential market for canned soft drinks possibly "double that of the current canned beer business," was foreseen by William C. Stolk, president of American Can Company, in announcing his company now is commercially producing a specially-designed flat-top can for carbonated beverages.

"It is still too early to make any firm predictions," Mr. Stolk said, "but if the consumer acceptance trends that have marked the success of the beer can are paralleled in the soft drink business then the volume of cans sold may eventually be twice that of the present beer can volume. This would mean between 12 and 13 billion soft drink cans a year."

The new container is similar in size and shape to the 12-ounce beer can which Canco first introduced just 20 years ago, he said. However, he added, extensive research and development work has gone into the perfection of the soft drink can to maintain the flavor and high carbonation of these products.

"This is not just another tin can," Mr. Stolk declared. "A number of technical problems, dealing with the chemical properties of various types of soft drinks and high internal pressures, had to be overcome before we could tailor a can that would adequately protect the same high quality of product the public has come to expect. At the same time it was necessary to design

a can that offered an attractive, convenient and durable package which could be mass produced economically."

To meet the technical considerations, he added, the company's research department developed specifications for the correct weight of tinplate, specially designed can ends, a new and stronger side seam and special inner coatings for added shelf life.

Initial production of the new can now is under way at the company's Hudson plant in Jersey City, Mr. Stolk said. He added that additional manufacturing lines are planned for installation at other company locations.

Although cans have been developed for a number of types of soft drinks, initial use of the new container was made in a marketing test in Rochester and Syracuse conducted by the Hoffman Beverage Company. The Pabst Brewing Company subsidiary recently introduced its new product, Tap-a Cola, in the New York metropolitan market.

American Can conducted successful tests with soft drinks in 1937, Mr. Stolk said, but material restrictions during and since World War II delayed marketing developments. Since then, he added, the company has been unwilling to enter the soft drink container business until technical and manufacturing considerations had been thoroughly researched and it had been determined that there would be wide consumer acceptance of canned carbonated beverages and sound economic advantages to all concerned.

The company has now studied all these factors and is confident both on the basis of its own research as well as reports from other sources, that conditions are favorable for entering the soft drink can market, he said.

"We base a large part of our confidence in the future of the soft drink can on our highly favorable experience with the beer can," he said. "The basic factors of convenience, protection and attractiveness which contribute so much to its success are equally applicable to the canned soft drink business."

Commenting on the company's plans for supplying container requirements in the growing canned

carbonated beverage market, Mr. Stolk said:

"We have every intention of expanding our facilities as we determine that consumer acceptance is in consonance with economic advantages for the beverage producer, the distributor, the retailer and ourselves. I am quite confident that by the end of the summer we shall be in a position to better measure the extent to which we should proceed with our manufacturing plans."

#### DR. SURREY OF STERLING-WINTHROP WRITES BOOK ON CHEMICAL NAME REACTIONS

Rensselaer, N. Y.—Dr. A. R. Surrey, senior research chemist at Sterling-Winthrop Research Institute here, is the author of a book on organic chemistry, just published by Academic Press, Inc., New York.

Title of the work is "Name Reactions in Organic Chemistry" (192 pp., \$4). It was written by Dr. Surrey to fill the need for a sharpened, up-to-date compilation of name reactions, one of the important tools of the organic chemist. These are the reactions designated by the names of the individuals who discovered or developed them, conforming with time-honored custom in chemical literature.

To the research chemist, name reactions are often an invaluable aid as basic source material to be applied, in varying degrees, in organic syntheses. Many have been modified over the years. Contributing to their development and improvement have been new procedures, reaction conditions, solvents and condensing agents.

In his treatment of the subject matter, Dr. Surrey describes each reaction, its scope, applicability and limitations, and brings it up to date in regard to new developments. Short biographical sketches of the "name chemists" are included.

Dr. Surrey graduated from the College of the City of New York with a B.S. degree and received his Ph.D. degree from New York University. He held a post-doctorate fellowship at Cornell University prior to coming to Winthrop Chemical Company, now Winthrop-Stearns Inc., in 1941. He later joined the Sterling-Winthrop Research Institute.

Dr. Surrey is the author or co-author of over 50 publications and patents dealing with organic syntheses. Included in his work is synthesis of the antimalarial Aralen (chloroquine), and the development of a process for its production. His most recent publication concerns synthesis of a group of new potent amebicidal agents.

#### INVITATION FOR VIII WORLD HEALTH ASSEMBLY MEET MEXICO CITY IN 1955 ACCLAIMED BY WHO COMMITTEE

The invitation of the Government of Mexico extended last year to the World Health Organization to hold its VIII annual assembly in 1955 in Mexico City was approved by acclamation by the VII World Health Assembly's Committee on Administration, Finance and Legal Matters. The invitation is subject only to confirmation by the Assembly in plenary session.

Appreciation was expressed by the Committee to the Government of Mexico, which has generously offered to bear all additional costs entailed in holding the Assembly outside of headquarters in Geneva. The Committee further noted that the Mexican Government had undertaken to extend "the necessary facilities, immunities and privileges" to all delegates, observers, members of the WHO secretariat and generally to all persons participating in the VIII Assembly.

It may be noted that all World Health Assemblies have been held at headquarters in the Palais des Nations in Geneva except the one held in Rome in 1949.

#### PARKE, DAVIS & COMPANY SEEKS TO HELP COMMUNITIES NEEDING A DOCTOR AND DOCTORS LOOKING FOR PLACE TO SETTLE

An advertisement sponsored by Parke, Davis & Company seeks to help small communities needing a doctor and young doctors looking for a place to settle.

The advertisement is headlined, "Does Your Community Need a Doctor? If so, the physician you're looking for may be the one who's looking for you!"

The copy points out, "Somewhere there is a doctor who would like to live in your community. He

may be completing his internship and looking for a place to settle. He may be a resident physician in a big city hospital, ready for a private practice. Or he may be a metropolitan specialist who longs for a chance to get closer to people—people like you, perhaps.

"Finding your doctor is one of the most important tasks your community can undertake. You stand to benefit not only from his professional services, but also from the contributions he'll make as a good citizen, from his participation in the life of the community."

The advertisement lists the questions a physician would like to know about the community, and concludes:

"Remember, the doctor you're looking for will want to live in your community for the same reasons that keep you there instead of somewhere else. When you have contacted him, tell him why you like your town. If he's the doctor who's looking for you, he'll be eager to join you for many long years of work, mutual benefit and happiness."

Parke, Davis & Company, whose

national advertising agency is Young & Rubicam, Inc., has been sponsoring "See Your Doctor" advertisements for the past 26 years.

### ALEVAIRE "MIST" MAKES TRACHEOTOMY UNNECESSARY IN LARYNGEAL DIPHTHERIA

Poplar Bluff, Mo.—The dramatic recovery of a 22-month-old child in acute respiratory distress from laryngeal diphtheria is attributed by a Missouri physician here to use of the drug Alevaire in dissolving viscid secretions in the air passages.

Dr. W. E. Henrickson reports in *Missouri Medicine* (51:202, Mar. 1954) that it is believed to be the first time Alevaire has been used to treat this condition. The patient's "prompt response" to the drug made it unnecessary to perform a tracheotomy, a procedure indicated in light of "extreme difficulty in breathing and pronounced cyanosis," he writes.

The child was admitted to the hospital in great respiratory distress, and was observed to have a croupy, harsh cough as well as forced and grunting expiration. Together with other symptoms revealed after examination, a diagnosis of laryngeal diphtheria was made, Dr. Henrickson relates. The child had not been immunized to the disease.

With a tracheotomy indicated, the child was placed in a croupette tent under oxygen. At this point, the doctor states, a nebulizing apparatus was attached to the tent and Alevaire was administered.


"Shortly after the vapor therapy was started, breathing became less labored and the child fell asleep."

The patient was later given antitoxin and penicillin at intervals. Marked improvement was noted at the end of eight hours under Alevaire and recovery was complete.

Introduced last year by Winthrop-Stearns Inc., Alevaire consists of an aqueous solution of a new non-toxic detergent in combination with other mucolytic ingredients. It has been found effective in a wide number of respiratory conditions in infants, including neonatal asphyxia, as well as in bronchial asthma in adults.

AMER. JOUR. DIG. DIS.

improve  
capillary  
resistance  
in prevention  
and treatment of  
capillary fragility  
capillary hemorrhage  
vascular accidents



# C.V.P.

(CITRUS FLAVONOID COMPOUND WITH VITAMIN C)

Five years of laboratory and clinical investigations establish the complete safety and value of C.V.P. in increasing capillary resistance and reducing abnormal bleeding due to capillary fragility.


C.V.P. provides natural bio-flavonoids (whole natural vitamin P complex) derived from citrus sources—potentiated by vitamin C—which act synergistically to thicken the intercellular ground substance (cement) of capillary walls, decrease permeability... and thus increase capillary resistance.

may protect against abnormal bleeding and vascular accidents in...

- hypertension
- retinal hemorrhage
- diabetes
- radiation injury
- purpura
- tuberculous bleeding

"Many instances of hemorrhage and thrombosis in the heart and brain may be avoided if adequate amounts of vitamin P and C are provided."

each C.V.P. capsule provides:	
Citrus Flavonoid Compound*	100 mg.
Ascorbic Acid (C)	100 mg.



bottles of 100,  
500 and 1000  
capsules

\*water soluble whole natural vitamin "P" complex, more active than insoluble rutin or hesperidin

USV

**u. s. vitamin corporation**  
 Casimir Funk Laboratories, Inc. (affiliate)  
 250 East 43rd Street, New York 17, N.Y.



# Meat...

## *and the Dietary Treatment of Gastrointestinal Disorders*

A recent study points out that patients with peptic ulcer, ulcerative colitis or regional enteritis can effectively utilize good quality protein from animal sources.\* Protein hydrolysates apparently are less effectively utilized than intact protein.

In patients with uncomplicated peptic ulcer on regimens providing intact animal proteins the patterns of amino acid excretion in urine and feces were similar to those in normal subjects. In patients with ulcerative colitis or regional enteritis the increased output of nitrogen and amino acids in the feces was attributed to loss of intestinal secretions, inflammatory exudate, and blood. Although the patients utilized intact animal proteins effectively, the authors suggested that an intake of more than one gram of dietary protein per kilogram of body weight might be useful.

On the basis of this study a dietary plan recommended for treatment of gastrointestinal disorders provides at least one gram, of protein per kilogram of body weight, but preferably more. Meat constitutes one of the important sources of animal protein in the plan.

In dietotherapy, meat serves many important physiologic and nutritional functions. Its appetizing flavor animates the desire to eat and promotes good digestion. Meat is easily and almost completely digested. Its high content of protein provides goodly amounts of all the essential amino acids well supplemented with others. Meat also contributes valuable amounts of many B vitamins and of essential minerals, especially iron, phosphorus, and potassium.

\*Kirsner, J. B.; Brandt, M. B., and Sheffner, A. L.: Diet and Amino Acid Utilization in Gastrointestinal Disorders, *J. Am. Dietet. A.* 29:1103 (Nov.) 1953.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.



**American Meat Institute**  
Main Office, Chicago...Members Throughout the United States



## NOTICE

In the June 1954 issue, the virtues of Nulacin for neutralizing gastric acidity were mentioned on page 173. It should be noted that Nulacin (Horlick) is obtainable in the United States as well as England.

### FREEZING SITE OF INJECTION FOUND TO RID CHILD'S FEARS

Gretna, La.—The often-hysterical fear of pain from an injection

experienced by some children can be eliminated in many cases by temporarily anesthetizing the site with a frozen solution of Zephiran, Dr. Ellen P. MacKenzie writes in the *Journal of Pediatrics* (44:421, April 1954).

Zephiran, manufactured by Winthrop-Stearns Inc., is a cationic detergent and germicide of high bactericidal and bacteriostatic potency. It is non-irritating to tissues in proper dilutions.

Noting that previous methods

employed by pediatricians were unsatisfactory, Dr. MacKenzie calls the skin cooling procedure with Zephiran both effective and simple. A 1:1,000 aqueous solution of Zephiran, with coloring material added for psychological effect, is poured into ordinary ice trays and placed in a refrigerator to freeze. The antiseptic properties of the solution are unchanged by freezing, she states.

Prior to injection, the area is rubbed with an ice cube until well chilled and "temporarily anesthetized," when the injection is given rapidly with a sharp needle.

The psychological reaction to piercing the skin is eliminated, as shown by the relieved laughter of older children who report "it didn't hurt" and return without fear for later injections, Dr. MacKenzie says. The technique was used with all patients old enough to fear injections, involving skin-puncturing procedures that did not require a dry field.

### BETA-METHISCHOL

U. S. Vitamin Corporation  
New York 17, N. Y.

multi-lipotropic  
palatable syrup

*Description:* a delightfully palatable, unusually comprehensive syrup, each fluid ounce (approx. 2 tablespoonfuls) provides:

Betaine Monohydrate .....	3.50 Gm.
Tri-Choline Citrate .....	1.40 Gm.
dl-Methionine (acetylated) ..	0.24 Gm.
Inositol .....	0.50 Gm.
Vitamin B <sub>12</sub> .....	24 meg.
Liver Concentrate .....	0.80 Gm.

*Action and Uses:* helps normalize fat and cholesterol metabolism, reduce elevated serum cholesterol levels and chylomicron-lipomicron counts . . . for specific therapy in reparable liver damage (cirrhosis, fatty infiltration, functional impairment, etc.); in obesity, hypertension, alcoholism, atherosclerosis, coronary occlusion, hypercholesterolemia.

*Administration:* 2 to 3 tablespoonfuls or more daily, in divided doses with meals.

*Supplied:* BETA-METHISCHOL Syrup—16 oz. and gallon bottles.

AMER. JOUR. DIG. DIS.



*Now...*  
new strength  
**Mesopin-PB**  
Tablets 5mg.  
homatropine  
methylbromide  
with 15 mg. pheno-  
barbital Also  
now available  
**Mesopin (plain)**  
5mg tablets.

for the "squeeze" of g.i. spasm

antispasmodic action  
virtually without atropinism . . .  
through the selective spasmolysis  
of homatropine methylbromide  
(one-thirtieth as toxic as atropine)  
plus the sedation of phenobarbital.

Each yellow tablet of MESOPIN-PB  
or teaspoonful of yellow elixir  
contains 2.5 mg. homatropine methyl-  
bromide and 15 mg. phenobarbital.  
Also available as  
MESOPIN Plain (without phenobarbital).  
in white tablets, green elixir, and powder.

**MESOPIN-PB**  
Homatropine Methylbromide and Phenobarbital

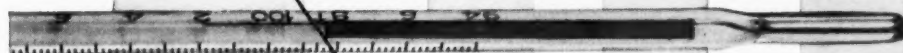
**Endo** Endo Products Inc.

Samples? Just write to:  
Endo Products Inc., Richmond Hill 18, New York

**when infection strikes...**



**and time is a factor...**



# ***Tetracyn***

Brand of tetracycline

*"... defervescence in  
temperature is  
... rapid with  
this new drug."*

In cases of infectious disease, time is a factor. Reports in a rapidly expanding body of literature emphasize that with Tetracyn therapy in susceptible infections, temperature promptly returns to normal—patients are often afebrile in hours.

Glatt and Ross<sup>2</sup> report that temperatures of patients with bacterial pneumonia "at the time of initiation of therapy ranged from 99.6 F to 105.2 F. ... In 3 children the temperature returned to normal within 24 hours after initiation of therapy [with tetracycline], in 7 within 24 to 48 hours, while only 2 cases required 72 hours before fever subsided."

1. Flippin, H. F.: Philadelphia Med. 49:788 (Jan. 30) 1954.
2. Glatt, M., and Ross, S.: Antibiotics & Chemotherapy 4:305 (Apr.) 1954.

*Whenever you take a temperature, for a prompt response with outstanding toleration—consider Tetracyn in susceptible infections.*

## ***Tetracyn***

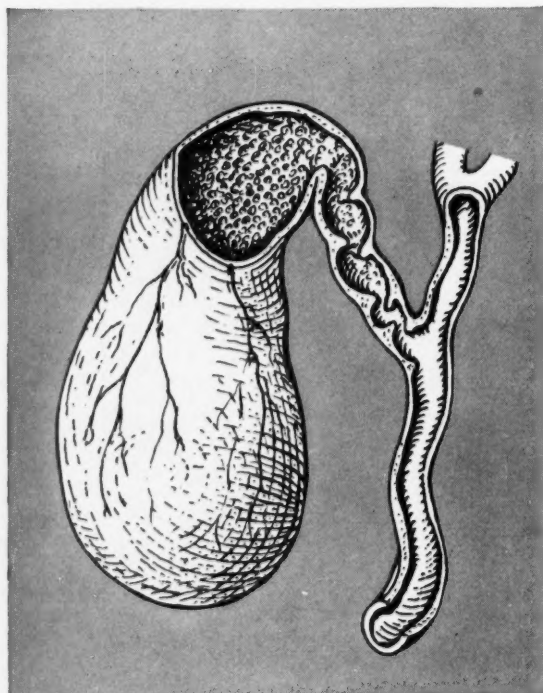
**BASIC ETHICAL PHARMACEUTICALS**  
536 Lake Shore Drive, Chicago 11, Illinois

**TABLETS (sugar coated)  
ORAL SUSPENSION  
INTRAVENOUS  
OINTMENT (topical)  
OPHTHALMIC OINTMENT  
PEDIATRIC DROPS  
CAPSULES**



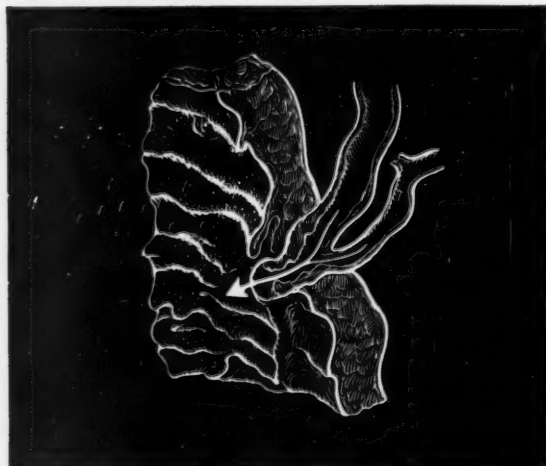
*By increasing bile secretion with Ketochol® and controlling sphincter of Oddi spasticity with Pavatrine®, a free flow of bile is instituted with resultant symptomatic improvement.*

## Conservative, Effective Medical Management of Chronic Gallbladder Disease



Gallbladder and ducts.

Ampulla of Vater and sphincter of Oddi.



The ketocholanic acids in Ketochol stimulate the flow of hepatic bile and flush the bile ducts. Antispasmodic medication, as provided in Pavatrine, diminishes gastrointestinal irritability and, by relaxing the sphincter of Oddi, effectively reduces symptoms of colic. This therapeutic program offers rational, conservative therapy in gallbladder dysfunction.

That the four bile acids present in Ketochol relieve biliary stasis is even more definitely proved by their use in the diagnosis of nonvisualized gallbladders. After the administration of Ketochol, the repeat cholecystograms permitted<sup>1</sup> correct diagnoses.

In conjunction with the foregoing medication, proper diet, adjusted intake of milk and cream and mental relaxation are important.

The average dose of Ketochol is one tablet three times daily with or following meals. The average dose of Pavatrine or Pavatrine with Phenobarbital is one or two tablets three or four times daily as needed. G. D. Searle & Co., Research in the Service of Medicine.

1. Berg, A. M., and Hamilton, J. E.: A Method to Improve Roentgen Diagnosis of Biliary Diseases with Bile Acids, *Surgery* 32:948 (Dec.) 1952.

Modern conception of liver cell.

